AN INTEGRATED PRACTICE OF MEDICINE

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A Complete General Practice of Medicine From Differential Diagnosis by Presenting Symptoms to Specific Management of the Patient

By HAROLD THOMAS HYMAN M D

1184 Illustrations 305 in Color
319 Differential Diagnostic Tables

W B SAUNDERS COMPANY
PHILADELPHIA AND LONDON

Reprinted October 1947 and April 1948

MADE IN U. S. A.

PRESS OF
W. B. SAUNDERS COMPANY
PHILADELPHIA

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THE BLOOD AND BLOOD FORMING ORGANS, INCLUDING THE SPLEEN

Associate Editors DANIEL STATS M D
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CHAPTER 48

NORMAL AND PATHOLOGIC PHYSIOLOGY

Cytology of Normal Adult Blood
Bone Marrow
Reticulo Endothel al System
Spleen
Lymph Nodes and Lymphatics
Physiology
Normal Variables in Hematology
Pathogenes s of Blood Disturbances

THE study of the circulating blood embraces a consideration of widely scattered anatomical structures whose relationships are apparent only through functional integrations The components include *blood cells bone marrow reticulo endothelial system spleen* and *lymph nodes*

CYTOLOGY OF NORMAL ADULT BLOOD

The peripheral circulating blood normally contains *erythrocytes* or red blood cells *g an ulocytes* or *leukocytes* of the neutrophilic eosinophilic or basophilic polymorphonuclear series small and large *lympl ocyt s monocytes* or mononuclear cells and *th ombocytes* or platelets

See F gs 227 228 and 229

BONE MARROW

Red and yellow marrow occupy the medullary cavities of th bones *Red marrow* s in a state of furct onal activity and gives rise to erythrocytes leukocytes and thrombocytes The red bone marrow possesses a central artery which gives into transitional capillaries and tufts of sinusoids which are o ly partially opened to the circulation When the s nusoids are completely collapsed the blood is stagnant oxygen tens on is d minished and red blood ll are produce l at a maximum rate (p 1010)

Yellow marrow is in a state of suspended animation It occup es most of the medullary spaces and is capable of transformation to acti e red marro when the need arises

RETICULO ENDOTHELIAL SYSTEM

The reticulo-endothel al system has medullary and extramedullary components In the bone marrow the reti ulum cells are representat ve of the system outside of the medullary cavity bes des the *Kupffer cells* of the liv r and the *clasmatocytes* elements are found i the *spl en* and in the *lymph* and *hem lymph nod s* and the pitu tary and adrenals

The cells of the t culo endothel al system are characterized by their *ph g cyt c b hat or* to certa n dyestuffs Funct onally they are concerned with (1) the format on of blood cells and bil rubin (2) the staining of fatty material (3) the phagocytic destruct on of blood cells (4) the formation of antibod es and (5) the metabolism of i on an l p gment

In the fetus the e tramedullary portions of the reticulo-endothel l system are of prime importanc in hematopo esis As a consequence neonatal disturban es of the blood are char acterized by marked enlargements of liver sple n and lymph nodes In the newborn and in infancy the marrow increasi gly assumes the primitive erythrogenic activities and extra medullary hematopo es s is enc ntered only as a pathological manifestation

SPLEEN

The anatomy of the spleen is el ewhere detailed (p 3559) The spleen has been described as a great reticulo-endoth lial sponge The circulatory pattern provides for slow or rap d transm ss on of blood The local out p m ts hematologic alterat ons of the



The rich vascularity of the organ indicates that it must be the site of great functional activity yet splenectomy is not associated with any notable changes

The indicated functions of the *normal spleen* include filtration a circulatory reservoir a site for antibody formation the delivery and denucleation of red cells the delivery and

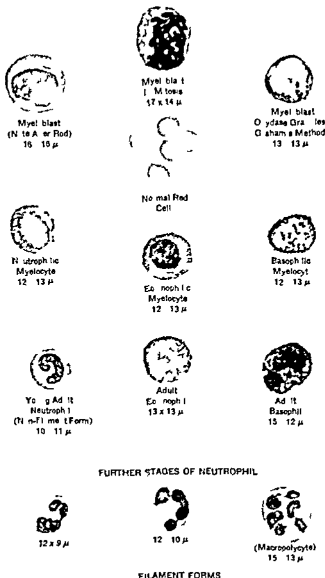


Fig 223—The white blood cells the granular or myelocytic series Wright's stain × 1000

maturation of white blood cells and platelets and the secretion of specific hormone as yet unidentified Additionally the *abnormal spleen* seems concerned with the destruction of red cells and platelets especially in chronic familial hemolytic anemia and chronic idiopathic thrombocytopenic purpura.

Pepper and Farley Practical Hematological Diagnosis

fluid and fulfils a reservoir function After the blood has traversed the arterioles it percolates slowly through the wide marshes of the splenic pulp and then is collected in the venous sinusoids The delayed flow affords opportunity for the exercise of splenic functions

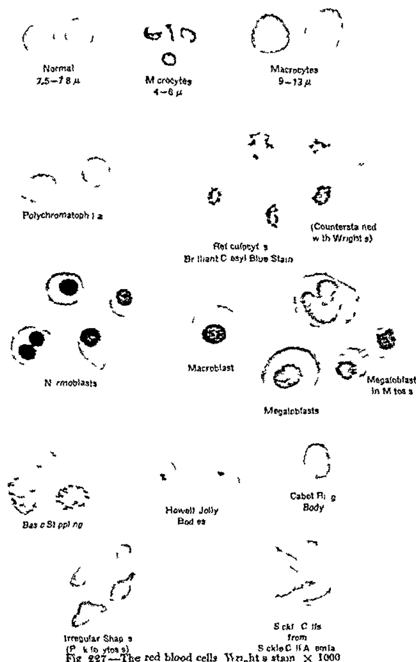


Fig 227—The red blood cells Wright's stain × 1000

and with extreme slowing and pooling of blood a considerable volume may be withdrawn from active circulation Blood also may be routed through the closed splenic circulation which serves as the "express track in contrast to the sluggish pulp route

Physiology—The physiology of the spleen remains one of the major medical mysteries

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Myeloblast
In Mitosis
17 x 14 μ

Myeloblast
(Not Auer Rod)
16 16 μ

Myeloblast
Oxydase Granule
Graham's Method
13 13 μ

Normal Red
Cells

Neutrophilic
Myelocyte
12 13 μ

Eosinophilic
Myelocyte
12 13 μ

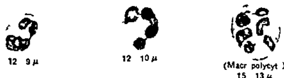
Basophilic
Myelocyte
12 13 μ

Young Adult
Neutrophil
(Non Filament Form)
10 11 μ

Adult
Eosinophil
13 13 μ

Adult
Basophil
15 12 μ

FURTHER STAGES OF NEUTROPHIL



12 9 μ

12 10 μ

(Macropolycyte)
15 13 μ

FILAMENT FORMS

Fig 228 —The white blood cells the granular or myelocytic series Wright's stain × 1000

maturation of white blood cells and platelets and the secretion of specific hormone as yet unidentified Additionally the *abnormal spleen* seems concerned with the destruction of red cells and platelets especially in chronic familial hemolytic anemia and chronic idiopathic thrombocytopenic purpura

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LYMPH NODES AND LYMPHATICS

The lymph nodes are glandular collections of lymphoid tissue with scattered reticulo endothelial elements They produce the lymphocytes of the circulating blood and function locally to filter out and immobilize foreign material collected by the regional lymphatic channels

Lymph tissue possesses remarkable powers of proliferation and hyperplasia so that *lymphadenopathy* is a common clinical response Enlarged lymph nodes that are not acutely inflamed are easily removed for direct histological investigation In acute inflammatory lymphadenitis puncture of the gland often reveals the causative organisms particularly in early syphilis

PHYSIOLOGY

Origin Maturation and Destruction of Erythrocytes—There is a considerable controversy among students of hematology as to the origin of the blood cells The unitarians consider that all cells are derived from the *hemocytoblast* a single primitive toti potential stem cell Other equally distinguished observers hold that each cell has an individual precursor and a separate cycle of maturation The controversy relative to *monophyletic* and *polyphyletic* concepts has only academic interest and need not concern the practitioner

Erythrogenesis—The endothelial lining of the vascular system of the red bone marrow is everywhere intact and is specialized to act as a precur or for the *erythroid cells* The adult non nucleated erythrocyte arises by maturation from *primitive cells* whose study is the concern of the specialist hematologist These precursors are *stem cells megaloblasts proerythroblasts normoblasts* and *reticulocytes* With the exception of the last named the primitive cells are nucleated They are observed in the peripheral blood only under abnormal conditions which require consultation with an expert

Maturation of the Blood Cells—Whereas the factors that govern the maturation of the other blood cells are at present unknown the orderly development of the red cells depends on a substance which is formed in the stomach and stored in the *liver* This *erythrocytic maturation factor* (E M F) is of the greatest clinical significance in hyperchromic macrocytic anemia

INTRINSIC AND EXTRINSIC FACTORS—The normal stomach secretes an intrinsic factor or *hematopoietin* without which normal hematopoiesis is impossible The substance is derived from the cardiac end of the human stomach It is thermolabile has some of the characteristics of an enzyme and reacts with the *extrinsic factor* which is present in certain proteins of lean muscle whole grain rice polishings egg and yeast extracts (marmite)

HEMATOPOIETIC PRINCIPLE OR ERYTHROCYTIC MATURATION FACTOR—The interplay between the intrinsic and extrinsic factors occurs in the stomach and small intestines The resulting product is absorbed from the ileum during which process it may or may not be altered It is carried in the blood stream to the liver kidneys and other organs where it is stored as the erythrocytic maturation factor or hematopoietic principle later to be used by the bone marrow in the process of hematopoiesis

MATURATION ARREST DUE TO DEFICIENCY OF HEMATOPOIETIC PRINCIPLE—The hematopoietic principle has a very definite function for the proper maturation of erythroid cells If it is present in inadequate amounts maturation arrest occurs at a very immature level and numbers of *megaloblasts* appear in the bone marrow With marked and prolonged deficiency of the hematopoietic principle the entire *bone marrow* becomes gelatinous red and laden with megaloblasts The normal constituents of the bone marrow are crowded out and are present in diminishing numbers Without liver extract therapy megaloblastic hyperplasia of bone marrow occasionally may progress to the development of an *aplastic state*

The hematopoietic principle may have functions other than maturation since its administration not only corrects the megaloblastosis but effects remarkable changes in gastro intestinal and neurological systems

Destruction of Red Blood Cells—The life of the normal erythrocyte is very limited and probably does not exceed a span of more than 10 to 15 weeks At the end of this time the worn-out red cell is phagocytized and destroyed by the cells of the reticulo endothelial system From this point on the pro ess cannot be followed morphologically but certain assumptions are warranted through information derived from the chemistry of hemoglobin as it is broken down to less complex products *The iron containing moiety* is stored and used anew for freshly manufactured red cells The remainder of the hemoglobin molecule is eventually transformed into *bilirubin* and transferred by the circulating blood to

the *liver* where it is excreted into the bil ary passages In the large intestines bilirubin is reduced by bacteria and 50 to 200 mg are excreted da ly in the stool as *fecal urobilinogen* The remainder of the urobil nogen is resorbed and most of this fraction is again used or again excreted by the li er into the bile A small fraction (1 to 2 mg daily) i lost as *urinary urobilinogen*

In the *hemolytic states* the bilirubin urobilinogen enterohepatic cycle is exaggerated If the liver is not capable of excreting the excessive amounts of b le p gment b lirubin accumu

LYMPHOCYTIC SERIES



Lymph bl t
16 x 16 μ



T k l tat
Fo m
14 15 μ



Lymph bl st
Sta ned for
O yd e G les
G ham s Method



14 13 μ



10 x 7 μ



8 7 μ



6 6 μ

Lymphocytes

MONOCYTIC SERIES



21 14 μ



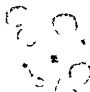
15 14 μ



13 12 μ



17 16 μ
(Mac oph ge)



Th mbocyte and
Red C ll

F g 229—The wh te blood cells Wr ght s stain × 1000

lates in the blood and eventually stains the tissues creating the cl ni al appearance of jaundice The increased serum bilirubin is attested by elevation of the i *terus ndex* (p 1943) the po itive *ind ect van den Bergh react on* (p 1947) and the excessi e *amounts of urobilinogen* in stool and urine (p 1948) The latter examinat ons are performed with facility and serve the pract t oner best for diagnos s and the est mation of the course of events

P pper and Farley Pract cal Hematological Diagnos s

Normal Economy of Blood Cellular Metabolism—This brief survey of the manner in which the blood cells are formed matured destroyed and regenerated serves to emphasize the enormity of the processes of erythrogenesis and the delicacy of the metabolic balance that must be established and maintained When it is realized that there are 5 000 000 red blood cells to the cubic millimeter and 5 000 000 000 to the cubic centimeter the numbers in the adult vessels reach astronomical proportions With an approximated 6000 cc of blood in the vascular channels the total figure for individual red cells in the adult circulating blood stream may be in the neighborhood of 30 000 000 000 000 If the life of the red cell is taken as twenty five days the daily destruction and regeneration of erythrocytes exceeds 1 000 000 000 000 or approximately 1 000 000 per second!

See *Anemias* (p 1055) *Polycythemias* (p 1092) See also Fig 228

Formation of the Granulocytes—The leukocytes are formed extravascularly in the bone marrow A fixed *reticulum cell* divides and produces a primitive free cell that is indistinguishable from the myeloblast In the process of maturation this cell assumes the appearance of a *myelocyte* Finally a *granulocyte* or *leukocyte* is formed and the granules take *neutrophilic eosinophilic* or *basophilic* stains

During the process of development the granulocytes develop *ameloid movement* and gain entrance into the lumen of the blood stream The newly formed cells become stored in the collapsed sinusoids of the bone marrow When these dilate the mature granulocytes are flushed into the peripheral circulation

See *Leukocytosis* (p 1096) *Leukemia* (p 1100) *Granulopenia* (p 1096) See also Fig 229

Formation and Destruction of Platelets—The thrombocytes or platelets probably arise from *megakaryocytes* which are giant cells of the extravascular bone marrow According to the accepted theory the platelets are pinched-off *pseudopodia* which protrude between endothelial cells of capillaries of bone marrow The destruction of platelets is probably associated with the function of the spleen for the removal of the spleen is often followed by a *thrombocytosis* The platelets function actively in blood coagulation a *thrombocytopenia* results in an increased tendency to hemorrhage See Fig 229

Formation of Lymphocytes—The lymphocyte originates from a *reticular cell* in the follicle of lymphoid tissue The primitive lymphoblast divides and forms large lymphocytes and finally mature lymphocytes Large and small lymphocytes are considered together as no useful purpose is fulfilled by separate discussion

See *Lymphocytosis* (p 1098) *Leukemia* (p 1100)

Formation of Monocytes—The monocyte originates from a *primitive reticular cell* of the spleen or connective tissues A primitive free cell is formed then a monoblast an intermediate monocyte and finally the mature monocyte

See *Infectious Mononucleosis* (p 1100)

Sites for Blood Formation—The clinical features of disturbances of the blood and blood forming organs are puzzling unless the practitioner recognizes the shifting sites for blood formation in fetal neonatal and adult life

BLOOD FORMATION IN THE FETUS—Fetal blood formation starts in the *mesoderm of the yolk sac* As the embryo develops *liver* and *spleen* assume important functions in hematopoiesis *At a later period of gestation marrow cavities develop and begin to participate in* blood formation As the marrow enlarges it assumes the greater proportion of hematopoietic function

BLOOD FORMATION IN INFANCY—In infancy all bones possess red bone marrow As the child grows functionally active marrow begins to diminish and by the seventh year it disappears gradually from extremity bones to be replaced by *yellow fatty marrow*

In infants and children an increased demand upon the marrow results in the resumption of primitive hematogenic activity by the extramedullary portions of the reticulo-endothelial system As a result the infantile blood dyscrasias are early characterized by enlargements of liver spleen and lymph nodes In the adult a similar but lesser extramedullary hematopoiesis occurs when medullary blood formation is inadequate for the need

BLOOD FORMATION IN THE ADULT—In the adult yellow fatty marrow increases in amount and *red marrow* is present only in sternum ribs and vertebrae bones of skull flat bones of pelvis and heads of femur and humerus The more extensive yellow fatty marrow fills the remainder of the cavities of long bones which provide potential reserve centers for hematopoiesis

With severe and prolonged demands upon red marrow yellow marrow becomes a t

vated and resumes its infantile erythrogenetic function So great may be the pressure of the expanding marrow that osseous lesions develop and rad ographs reveal demonstrable areas of bone absorption When marrow activity is no longer competent to maintain the normal status of the circulating blood extramedullary hematopoies s is resumed and spleen liver and lymph nodes enlarge

See *Splenomegaly* (p 1129) *Hepatomegaly* (p 1973) *Lymphadenopathy* (p 1156)

NORMAL VARIABLES IN HEMATOLOGY

The interpretation of blood counts requires that allowances be made for technical factors and physiological variables such as age pregnancy digestion altitude temperature and exercise

Infancy—The hemogram of the infant differs in many striking respects from that of the adult Failure to recognize this fact may lead to errors in diagnosis prognosis and therapy

Red Count—At birth the red blood count averages 5 000 000 cells but the extremes vary between 4 000 000 and 9 000 000 per cu mm Wh le these variations are partially physiological it is quite likely that technical considerations are of greater s gnificance The pla centa contains one f fth to one fourth of the total fetal blood If the umbilical cord is clamped immediately after birth the child is deprived of this blood mass A delay of ten minutes before clamping permits the contracting uterus to transfuse" the placental blood into tl e circulation of the infant and appreciably increases red cell volume and hemoglobin content

See *Anemias of the Newborn* (p 2738)

Blood Smear—The ind vidual erythrocytes of the newborn sl ow variations in size and shape with a tendency to *macrocytosis* In addition to macrocytes as many as 2000 *normoblasts* per cu mm are normally present The normal normoblastosis is not to be confused with the changes in erythroblastosis foetalis (p 1067)

Tl e *reticulocyte count* approximates 2 per cent and tends to rise to 3 per cent by the end of the tl ird month Normoblasts disappear more rapidly than reticulocytes and are rarely present beyond the second week

Hemoglobin—The absolute hemoglobin content of the red cell is hi her in the newborn than at any other period of l fe The average reading by the Hal lane method (p 3634) approximates 145 per cent with a fall to "5 per cent at three months and a rise to 80 or 90 per cent by the end of the first year

Leukocyte Count—The leukocyte count at birth averages 18 000 cells per cu mm There is a rap d decrease during th first week but a secondary rise to the original level about the twelfth day The original leukocytosis is caused by an increa e in the *polymorphonu lear neutroph ls* while the secondary increase is due to a *lymphocytosis* These phenom na are not to be interpreted as ind cations of infection

Platelet Count and Prothrombin Level—The platelet count is very little altered from that of the adult but there is a *prothrombin deficiency* during the first few days of l fe giving rise to a physiological prolongation of the coagulation time Excessive hypoprothrombinemia produces the *hemorrhagic disease of the newborn* See p 1111

Hematopoiesis—At b rth the hematopoietic functions shift from the extramedullary centers to the bone marrow A new equil brium between blood formation and blood destruc tion is established and the e cess of hemoglobin which is required in intra uterine life is necessarily destroyed Consequently there may be an overproduction of bilirubin resulting in the phys ological jaund ce of the newborn (icterus neonatorum)

Many infants experience a lag in medullary erythropoiesis hence a moderate degree of *pl ysiological anemia* is often seen toward the end of the neonatal period This disturbance increases gradu lly to reach its full intensity by the end of the second or third month In all likelihood early clamping of the umbil cal cord is an important accessory factor in the gene s of the pl ys ological anemias particularly in prematures

P g an y—Dur ng pregnancy the *hemoglobin* level falls to approx mately 10 gm per 100 cc the *red count* may be as low as 4 000 000 A considerable *leukocytosis* approxi mating 15 to 25 000 cells per cu mm is usually present during tl e last month of pregnancy and at th t me of delivery This elevation of the white count is not due to infection and is not ind cative of a seps s

D gest —D gestion produces a sl ght rise in *leukocytes* The afternoon tide of leukocytes wh ch reaches a maximum four hours after feeding is probably a manifestation of the d ge tive cycle and is most apt to occur after a meal rich in protein

Widal's Hemoclastic Crisis—Exceptions to the postdigestive leukocytosis occur in liver disease and the allergic states In the former following a protein meal of 200 cc of milk a slight *leukopenia* is noted in twenty to forty minutes This phenomenon which is associated with a fall in blood pressure and a prolonged coagulation time is known as *Widal's hemoclastic crisis*

The Leukopenic Index—In the allergies ingestion of the exciting foods may give rise to a leukopenia This leukopenic index is of significance only when the fluctuations exceed 50 per cent in the total white count or 10 per cent in the differential estimation

Altitude—With diminution in oxygen tension at high altitudes compensatory increases in the red blood-cell counts and the hemoglobin readings are noted The phenomenon is one of physiological *polycythemia*

High Temperature—During periods of a great loss of fluid caused by sweating there is a diminution in plasma volume and a secondary *hemoconcentration* This change is rapidly reversible when lost fluid is replaced

A *polymorphonuclear leukocytosis* is of regular occurrence after exposure to high fever This is an advantageous defensive mechanism in *hyperthermia*

Exercise—A marked increase in the leukocyte count may occur during muscular exercise White counts as high as 35 000 per cu mm may result from the violent muscular contractions in convulsive episodes The leukocytosis at the time of delivery may be of similar mechanism

THE MARROW COUNT

Specimens of red marrow are obtained by sternal puncture *Under normal circumstances* the marrow count approximates 120 000 nucleated cells per cu mm Of these about 70 per cent are white blood cells and their precursors and 30 per cent are young erythroid elements Normally there are 22 to 66 megakaryocytes per cu mm In a simplified and schematic form the appended chart gives the normal findings and the common deviations under pathological conditions

Mechanisms of Abnormalities in the Marrow—The factors that cause hyperplasia and hypertrophy of bone marrow are not always definable With respect to the red cells a potent and frequent stimulus is a *decrease in the numbers of circulating erythrocytes* Hyperactivity of bone marrow also results from deficiency in erythrogenic constituents under which circumstance imperfect cells are produced For example when the *hematopoietic principle of liver extract is absent or diminished* the maturation of the red cells is arrested at the megaloblastic stage As a result there is a disordered erythropoiesis the marrow contains an abnormal number of megaloblasts and the peripheral circulation is flooded with macrocytes

With an *inadequate supply of iron* the bone marrow is disturbed in the normoblastic and erythroblastic phases the cells are deficient in hemoglobin as recognized by their lessened pigment content The circulating erythrocytes as contrasted to the hyperchromic macrocytes of pernicious anemia are hypochromic and microcytic

Other essential building factors for hemoglobin or red blood cell development include *copper cobalt porphyrins* various *amino acids thyroxin* and vitamin A and pyridoxine The exact functions of these accessory factors are unknown at the present time

PATHOGENESIS OF BLOOD DISTURBANCES

The circulating blood delicately reflects almost every significant variation that occurs in the human economy Indeed broader hematological studies result in an increasing recognition of the fact *that there are few intrinsic blood disorders* Even *primary or pernicious anemia* is now recognized as a deficiency in the erythrocyte maturation factor *agranulocytosis or malignant neutropenia* is no longer regarded as a blood dyscrasia but is usually due to a sensitivity to aminopyrine *hemorrhagic disease of the newborn* is a vitamin K deficiency *hemorrhagic purpura* results from the destruction of platelets by drugs and chemicals *icterus gravis* is concerned with the inheritance of agglutinating antibodies

These more intelligible concepts of the disturbances of the blood call for a revaluation of descriptive hematology In the morphological or his

TABLE 68 —THE BONE MARROW IN NORMAL AND PATHOLOGIC CONDITIONS
(Numbers are per cu mm The boldface figures are of greatest diagnostic significance)

	Normal	Acute Myelogenous Leukemia	Chronic Myelogenous Leukemia	Chronic Lymphatic Leukemia	Pernicious Anemia	Hemolytic Anemia	Aplastic Anemia	Polycythemia Vera	Multiple Myeloma	Agranulocytosis	Infectious Mononucleosis
Total nucleated cell count	120 000	750 000	500 000	500 000	150 000	750 000	**10 000**	100 000	100 000	100 000	200 000
Myeloblasts	1	**90**	10	5	5	1	0	1	1	5	2
Myelocytes	20	10	**70**	10	15	15	5	20	25	**30-50**	30
Polymorphonuclear leukocytes	50	5	15		30	5	70	60	30	**0**	35
Lymphocytes	5	2		**80**	10	1	15	2	5	20	10
Normoblasts	20	3	4	5	10	**60**	5	15	14	20	20
Erythroblasts	2		1		10	**15**	1	2	1	2	2
Megaloblasts	—				**20**	5					
Plasma cells	0 5						4		**25**	5	

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CHAPTER 49

GENERAL METHODS OF DIAGNOSIS AND TREATMENT OF DISEASES OF THE BLOOD AND BLOOD FORMING ORGANS

DIAGNOSIS

The diagnosis of disturbances of the blood and blood forming organs may require investigation of blood serum bone marrow urine stool gastric contents lymph nodes and long bones

In Table 69 the required tests are enumerated and references are given to technical details normal values are included as well as indications for the performance of each test

METHODS OF TREATMENT IN DISEASES OF THE BLOOD AND BLOOD FORMING ORGANS

The practitioner has many resources at his disposal in the treatment of disease of the blood and blood forming organs They include drug therapy diet transfusion irradiation and surgical procedures

Drug Therapy

The drugs and biologicals used in the treatment of diseases of the blood include hematinics anti anemic principles hemolysins leukocyte stimulants leukocyte depressants coagulants and anticoagulants

ANTICOAGULANTS

Anticoagulants are agents that retard or prevent the coagulation of the blood Inorganic substances such as the salts of *citric* and *oxalic acids* are extremely valuable in the prevention of coagulation in vitro but cannot be used systemically the *citrate* ion is destroyed in the body while the *oxalate* radical which produces acute hypocalcemia is too toxic for systemic use

Organic compounds which prevent blood coagulation are *heparin hirudin* and a number of complex polysaccharides and synthetics chiefly *dicoumarol* and *azo dyes* (thiazole pink) There is increasing evidence of the

torical era clinical abnormalities were labeled with the name of the physician who described the derangement or else they bore a Latin or Greek translation of the presenting sign or complaint Thus the appended glossary (p 4052) lists such references as Biermer's anemia Addison s anemia Chauffard Minkowski's disease Cooley s anemia Geisbock s disease Hand Christian Schuller syndrome icterus gravis (severe jaundice) hemorrhagic purpura (bleeding with black and blue spots) and acholuric jaundice (yellow discoloration without bile in the urine)

Practical therapy is encouraged by discarding the academic features of descriptive hematology Recognition of the fact that most hematological disorders are reflections of some distant disturbance often points the way to the prevention and alleviation of the affliction The principal culprits are mechanical agencies chemical and pharmacological sensitizations and intoxications metabolic derangements and the infections

Mechanical Disturbances —A common cause for anemia is *blood loss* that may result from acute hemorrhage or chronic and continuous bleeding

Chemical and Pharmacological Sensitivities and Intoxications —Chemical and pharmacological agents often provoke disturbances of the hematopoietic system Anemias occur in chronic *lead and benzol poisonings* hemolytic and aplastic anemias and thrombocytopenia result from the use of the *arsenicals* fatal agranulocytosis may be encountered from *aminopyrine* widespread hematological phenomena are encountered in chemotherapy with the *sulfonamides*

Metabolic Changes —Many of the disturbances of metabolism are reflected in the blood An *eosinophilia* is characteristic of allergy *lymphocytosis* occurs characteristically in hyperthyroidism an *anemia* is often a persistent finding in hypothyroidism *deficiency of vitamin K* produces a hemorrhagic disease due to prothrombin deficiency *lack of vitamin C* gives rise to the characteristic capillary fragility of scurvy

Infections.—Infections cause a wide range of alterations in the blood picture Most suppurative processes are accompanied by a *polymorphonuclear leukocytosis* but a *lymphocytosis* characterizes typhoid fever and pertussis The prolonged infections produce changes in the red cells *anemias* are associated with prolonged sepsis particularly those caused by hemolytic streptococci

TABLE 69.—LABORATORY AIDS IN THE DIAGNOSIS OF DISTURBANCES OF THE BLOOD AND BLOOD FORMING ORGANS (Continued)

Tests whose names appear in capital letters may be made by the practitioner in his office laboratory those which appear in normal size type are best referred to the clinical pathologist for expert opinion

Test	Technic	Normal Values	Indications
Blood Volume		70 to 90 cc. per kilo of body weight	Shock polycythemia
BLOOD GROUPING AND MATCHING	p 3708		Transfusion paternity tests
Rh Factor	p 1067	Test with anti Rh serum	Erythroblastosis foetalis repeated transfusions transfusion in pregnancy
Donath Landsteiner Reaction	p 1075		Paroxysmal hemoglobinuria
Acid Hemolysis Test	p 1070		Nocturnal hemoglobinuria
Cold Agglutinins	p 3711		Blood matching primary atypical pneumonia
Red Cell Diameter			Hypochromic anemia and hyperchromic anemia
Blood Bilirubin	p 1948		Hemolytic anemias
Icterus Index	p 1949		Hemolytic anemias
Van den Bergh Reaction	p 1947		Hemolytic anemias
Heterophile Reaction	p 468		Infectious mononucleosis
Bone Marrow Smears	p 1043	Table 68	Anemias leukemia reticulo-endotheliosis multiple myeloma agranulocytosis and infectious mononucleosis
Lymph Node Biopsy	p 1136		Leukemia diseases of the lymph nodes
BLOOD AND BLOOD PIGMENT IN URINE	p 3693		Hemolytic anemias and hemoglobinurias
BILE AND BILE PIGMENTS IN URINE (UROBILIN AND UROBILINOGEN)	p 3686		Hemolytic anemias
BLOOD IN STOOL	p [illegible]28		Secondary anemia
UROBILINOGEN IN STOOL	p 1948		Hemolytic anemias
GASTRIC CONTENT	p 3721		Anemias
Radiography of Long Bones	p 1134		Reticulo-endothelioses

TABLE 69.—LABORATORY AIDS IN THE DIAGNOSIS OF DISTURBANCES OF THE BLOOD AND BLOOD FORMING ORGANS

Tests whose names appear in capital letters may be made by the practitioner in his office laboratory those which appear in normal size type are best referred to the clinical pathologist for expert opinion

Test	Technic	Normal Values	Indications
HEMOGLOBIN	p 3694	Men 14 to 16 gm per 100 cc women 13 to 15 gm per 100 cc	Routine in all hematologic disorders
RED CELL COUNT	p 3698	Men 4 6 to 6.2 million women 4 2 to 5 4 million per cu mm	Routine in all hematologic disorders
WHITE CELL COUNT	p 3698	5000 to 10 000 per cu mm	Routine in all hematologic disorders
PLATELET COUNT	p 3698	150 000 to 400 000 per cu mm	Routine in all disturbances of blood coagulation
BLOOD SMEARS	p 3699	Neutrophils 50 to 70% lymphocytes 25 to 35% monocytes 2 to 8% eosinophils 1 to 4% basophils 0.5 to 1%	Routine in all hematologic disorders
COLOR INDEX	p 3705	0 8 to 1 0	Routine in all hematologic disorders
MICROSCOPY OF FRESH BLOOD	p 3699	Biconcave disks	Sickle cell anemia target cell anemia and erythroblastic anemia of Cooley
RETICULOCYTES	p 3705	Up to 2 per cent	Hyperchromic anemia hemolytic anemia therapy with liver extract
BLEEDING TIME	p 3706	1 to 4 minutes	Hemorrhagic conditions
COAGULATION TIME	p 3706	8 to 15 minutes	Hemorrhagic conditions treatment with heparin
Prothrombin Time		15 to 20 seconds	Hemorrhagic conditions Vitamin K deficiency treatment with dicoumarin
CLOT RETRACTION	p 3706	1 to 24 hours	Hemorrhagic conditions
FRAGILITY OF RED CELLS	p 3706	0 44% to 0 30% saline	Hemolytic anemia
Peroxidase Stain			Leukemia
SEDIMENTATION RATE	p 3707	18 mm in 1 hour	Infections
Hematocrit Determination	p 3707	Men 40 to 54 % women 37 to 47 %	Hemoconcentration hemodilution shock
CAPILLARY FRAGILITY	p 3708	Less than 10 petechiae	Hemorrhagic diatheses vitamin C deficiency
Plasma Volume		40 to 50 cc per kilo of body weight	Shock polycythemia

TABLE 69.—LABORATORY AIDS IN THE DIAGNOSIS OF DISTURBANCES OF THE BLOOD AND BLOOD FORMING ORGANS (*Continued*)

Tests whose names appear in capital letters may be made by the practitioner in his office laboratory those which appear in normal size type are best referred to the clinical pathologist for expert opinion

Test	Technic	Normal Values	Indications
Blood Volume		70 to 90 cc per kilo of *body weight*	Shock polycythemia
BLOOD GROUPING AND MATCHING	p 3 08		Transfusion paternity tests
Rh Factor	p 1067	Test with anti Rh serum	Erythroblastosis foetalis repeated transfusions transfusion in pregnancy
Donath Landsteiner Reaction	p 10 5		Paroxysmal hemoglobinuria
Acid Hemolysis Test	p 1076		Nocturnal hemoglobinuria
Cold Agglutinins	p 3711		Blood matching primary atypical pneumonia
Red Cell Diameter			Hypochromic anemia and hyperchromic anemia
Blood Bilirubin	p 1948		Hemolytic anemias
Icterus Index	p 1948		Hemolytic anemias
Van den Bergh Reaction	p 1947		Hemolytic anemias
Heterophile Reaction	p 4f8		Infectious mononucleosis
Bone Marrow Smears	p 1043	Table 68	Anemias leukemia reticulo-endotheliosis multiple myeloma agranulocytosis and infectious mononucleosis
Lymph Node Biopsy	p 1136		Leukemia diseases of the lymph nodes
BLOOD AND BLOOD PIGMENT IN URINE	p 3683		Hemolytic anemias and hemoglobinurias
BILE AND BILE PIGMENTS IN URINE (UROBILIN AND UROBILINOGEN)	p 3686		Hemolytic anemias
BLOOD IN STOOL	p 3 8		Secondary anemia
UROBILINOGEN IN STOOL	p 1948		Hemolytic anemias
GASTRIC CONTENT	p 3721		Anemias
Radiography of Long Bones	p 1134		Reticulo endothelioses

TABLE 70—DRUG THERAPY IN BLOOD DISEASES

Preparation	Dose	Therapeutics
Reduced Iron U.S.P	1 to 1.5 gm daily in capsules or compressed tablets	Hematinics in hypochromic anemia inorganic preparations as efficacious as organic ferric salts converted to ferrous compounds and absorbed similarly utilization favored by the simultaneous administration of hydrochloric acid and/or the bile salts No advantage from parenteral injection may cause transitory abdominal pain with diarrhea or constipation stools appear black and give a false positive reaction for blood
Iron and Ammonium Citrate U.S.P	*4 to 8 gm daily in* capsules	
Iron and Sodium Citrate	4 to 8 gm daily in capsules	
Ferrous Sulfate U.S.P	1 to 2 gm daily in pills or tablets	
Pills of Ferrous Carbonate U.S.P (Blaud Pills)	2 to 4 gm daily	
Mass of Ferrous Carbonate U.S.P	3 to 6 gm daily in capsules	
Antihemophilic fraction of Human Plasma	5 to 10 cc	Hemophilia
Nitrogen Mustards	0 1 mg per kg	Hodgkin s disease
Extract of Liver U.S.P	Powder or capsule for oral use (12 to 20 gm equals 1 oral unit)	Anti anemic principles for use as hematinics in hyperchromic macrocytic anemia (p 1017) *U.S.P unit is minimum amount which when given daily to a suitable patient* with pernicious anemia in relapse will cause an adequate hematopoietic response the requirement is 30 times more orally than by injection responses followed by hemogram and reticulocytes May produce eosinophilia
Extralin N.N.R	Liver-stomach concentrate in pulvules for *oral use (12 pulvules equal 1 oral unit)*	
Powdered Stomach U.S.P (Ventriculin)	For oral use (40 gm equal 1 oral unit)	
Solution of Liver U.S.P	Liquid for oral use (45 cc equals 1 oral unit)	
Liver Injection U.S.P	Solution for intramuscular injection (1 to 15 U.S.P injectible units per cc)	
Hydrochloric Acid U.S.P	2 to 4 cc in water through glass drinking tube	To assist the utilization of iron in hypochromic anemia for anacidity in hyperchromic anemia
Bile Salts N.N.R	Capsules 0.2 gm	To assist utilization of iron in hypochromic anemia to facilitate absorption of menadione in vitamin K deficiency
Glycotauro N.N.R	Tablets 0 078 gm	
Dehydrocholic Acid N.N.R	Tablets 0.25 gm	
Sodium Dehydrocholate N.N.R	Ampules (20 per cent)	

TABLE 70.—DRUG THERAPY IN BLOOD DISEASES (*Continued*)

Preparation	Dose	Therapeutics
Phenylhydrazine Hydrochloride	Capsules 0 2 gm daily for 3 or 4 days	For destruction of excessive numbers of red cells in polycythemia vera Check by frequent blood counts as over dosage may lead to serious anemia with renal and hepatic damage
Acetyl phenyl hydrazine (Pyrodin)	Capsules 0 1 gm daily for 3 or 4 days	
Solution of Potassium Arsenite (Fowler's Solution) U.S.P	Drop doses according to blood count	In polycythemia vera and in leukemia to cause reduction of excessively high blood counts Check with frequent hemograms
Radioactive Phosphorus (P 32)	3.5 to 4 0 millicuries	For destruction of abnormal numbers of red and white cells respectively in polycythemia vera and leukemia Check by frequent hemograms
Pentonucleotide N.N.R	10 cc contain 0 7 gm , give intramuscularly twice daily	For stimulation of leukocytes in agranulocytosis
Adenine Sulfate	Freshly prepared solution of 1 to 2 gm in physiological saline; intramuscular injection of 30 to 50 cc	
Calcium Salts	p 603	Used ineffectually as coagulants in the bleeding diatheses
Brain Lipoid N N.R	Local use	As coagulants in bleeding from accessible surfaces on skin or mucous membranes
Fibrogen	Local use	
Solution Brain Extract N N.R (Thromboplastin)	Local use	
Snake Venom (Russell Viper)	Local use (1/10,000)	
Menadione U.S.P	1 to 2 mg in tablets or ampules	For specific coagulant therapy in vitamin K deficiency such as hemorrhagic disease of the newborn jaundice and diarrheal conditions
Ascorbic Acid U.S.P	0 15 gm	To correct capillary fragility due to specific deficiency of vitamin C
Folic Acid	10 to 30 mg	Macrocytic anemias
Heparin	See p 1050	Effectual anticoagulant
Dicoumarol	See p 1051	Effectual anticoagulant
Blood Plasma	25 to 500 cc	Forward failure with hemoconcentration
Fibrin Foam Oxidized Cellulose (Oxycel) and Topical Thrombin	Local application	Hemophilia and surgical bleeding especially those associated with jaundice
Citrated Blood	500 cc	Anemia
Penicillin	20 000 to 100 000 units	Agranulocytosis

value of these preparations in the prevention and treatment of *intravascular thrombosis* (p 1123), and *embolism* in *vascular surgery* and *peripheral vascular disease* and in combination with penicillin for the cure of *subacute bacterial endocarditis* (p 1021)

HEPARIN

Heparin a normal constituent of the circulating blood acts as a physiological antagonist to prothrombin in blood coagulation It is obtained chiefly from liver but is also present in lung and skeletal muscle

Pharmacology—Heparin prolongs the coagulation of blood in vivo and in vitro by a mechanism whose exact action has not been established Apparently the compound inhibits the conversion of prothrombin to thrombin and the agglutination of blood platelets The effect on blood coagulation appears immediately and persists for a variable period after an effective dose The heparin action may be completely inhibited by certain proteins such as protamine which neutralize its electronegative charge

The exact chemical structure of heparin is not known but in all likelihood it is a complex polysaccharide containing glucosamine It is probably a tetrasaccharide with 2 molecules of N acetyl glucosamine 2 molecules of glycuronic acid and 5 sulfuric acid ester groups The substance has been isolated in crystalline form as barium sodium and ammonium salts

Therapeutics—Heparin cannot be administered orally since it is destroyed in the stomach To maintain a prolongation of the coagulation time for an extended period requires that the drug be given *intravenously* in a continuous infusion or *subcutaneously* using a slow acting preparation recently introduced by Loewe

The administration of heparin by *continuous intravenous drip* may be accomplished with a total volume of 1000 cc of fluid in 24 hours The degree of prolongation of coagulation time may be varied by changes in the speed of administration or by variations in the concentration of heparin in the infusion Cessation of the continuous venoclysis results in a return of the coagulation time to normal in a few hours An abrupt termination of the incoagulable phase may be induced by the transfusion of fresh blood or the administration of protamine The chief drawback to this method of therapy is its excessive cost

The heparin dose required to produce a given degree of prolongation of coagulation time varies in different individuals since patients may be *heparin sensitive* or *heparin resistant* A dose of 20 mg per hour by continuous intravenous drip produces an adequate prolongation of the coagulation time to 30 minutes or 1 hour in the average adult patient In order to obtain the desired effect the clotting time must be determined every 3 or 4 hours and the dose increased or decreased accordingly To obtain rapid heparinization an initial dose of 40 to 60 mg in a small volume of solution (10–20 cc) is usually sufficient Most heparin preparations available for systemic use are distributed in vials containing 10 mg per 1 cc Each mg is equal to 100 Toronto units

The heparin unit of potency is the activity represented by 0 01 mg of the purest heparin a crystalline barium salt prepared at the Connaught Laboratories in Toronto This unit is 5 times as large as the original

Howell unit which prevented the clotting of 1 cc of cold cat s blood for 24 hours

The *subcutaneous implants* advocated by Loewe are made with a solution of heparin in a vehicle composed of gelatin glacial acetic acid glucose and water (Pitkin menstruum) The contents of an ampoule are liquefied at 55 C drawn up through a 2½ inch 19 gauge needle into a previously warmed sterile 5 or 10 cc syringe and immediately injected subcutaneously or subfascially into the anterior or lateral aspect of the thigh The injection mass congeals promptly after inoculation producing local pain and an occasional systemic reaction Heparinization is rapidly intiated with 200 to 400 mg of the drug and is maintained with smaller amounts at spaced intervals With this technic no prompt termination of the heparin effect is as yet feasible Whole blood transfusion or prota mine may be employed to neutralize the free heparin while compression about the site of inoculation will retard its further liberation The chief advantages of the Loewe method are the ease of administration and the reduction in the amount of required heparin

Toxicity—Hemorrhagic phenomena are the only untoward effects at tendant on the use of purified crystalline preparations of heparin Hema turia purpura epistaxis and internal hemorrhages often seen in intrave nous dosage are strikingly absent with the Loewe preparation which is distinctly the product of choice

DICOUMAROL

Dicoumarol is the cause of a hemorrhagic disease in cattle that have eaten spoiled sweet clover The substance was isolated from spoiled sweet clover by Link and was later synthesized by his group It differs from heparin in being active after oral administration and in lacking an anti coagulant action in vitro Dicoumarol is a complex organic compound con taining the benzene ring it is easy to synthesize and may be produced inexpensively The disodium salt is water soluble

Pharmacology—The administration of dicoumarol leads to a prolonga tion of prothrombin and coagulation times The action of the drug is pre ceded by a latent period of 24 to 72 hours The mechanism of action is not definitely known but it is suspected that the drug inactivates *vitamin* K or inhibits the formation of *prothrombin* by the liver

Mode of Administration—Dicoumarol is effective after oral adminis tration The disodium salt may be given intravenously to patients who fail to respond to oral doses due to a failure of absorption

Dosage—The initial oral dose of dicoumarol approximates 2 mg per pound of body weight but the total dose should not exceed 400 mg (6⅔ grains) Subsequent doses depend on the results of prothrombin and coag ulation time determinations which should be done daily If no effect is observed 300 mg (5 grains) are given on the third day but if a marked effect is obtained the drug is withheld A satisfactory response is a pro longation of the clotting time to within 20 to 25 minutes and a fall in the prothrombin index to between 30 and 50 per cent As a rule the in crease in coagulation and prothrombin times is in direct proportion to the size of the dose Prolongation of the clotting time beyond 30 minutes is dangerous and may cause multiple bleedings Following the discontinu

ance of the drug it may require 1 to 2 weeks for the prothrombin time to return to normal

Toxic Manifestations —The use of dicoumarol is attended occasionally by nausea vomiting and lumbar pain hemorrhagic phenomena are common and include *hematuria epistaxis purpura* and *hemorrhage* at the site of an operative wound Repeated blood transfusions are of little value in arresting hemorrhage induced by dicoumarol but the action of the drug may be somewhat neutralized by 60 mg doses of menadione There is no evidence of any interference with liver function following the use of dicoumarol other than the impairment of prothrombin formation A sudden increase in the blood sedimentation rate is a reliable sign of hemorrhage in a patient receiving dicoumarin

Dicoumarol versus Heparin —It is our opinion based on experience that subcutaneous implants of heparin constitute the anticoagulant therapy of choice Intravenous heparin is cumbersome and expensive dicoumarol despite its advantage of low cost and its adaptability for oral administration is slow to show its effects considerably more toxic more difficult to control and more difficult to correct in comparison to the Loewe preparation of heparin which we regard without qualification as the remedy of first choice

DIETOTHERAPY

A high iron high vitamin diet is of some value in the treatment of malnutrition pregnancy the anemias hemorrhage chronic infection and prolonged debilitating disease *A type diet is undernoted*

HIGH IRON—HIGH VITAMIN DIET

Indications —*Malnutrition pregnancy anemias hemorrhage chronic infections* and *debilitating diseases* of long standing all suggest the need for high iron high vitamin diet

Adjuvants —In addition to dietary control it is usually wise to use iron salts and vitamin concentrates as supplements

Type Diet

BREAKFAST

Glass of fruit juice
Stewed or raw fruit
Oatmeal wheatena or any whole grain cereal
Egg
Whole wheat bread with butter
Milk or cocoa.

MIDDAY MEAL OR SUPPER

Cream soup or vegetable soup
Liver or lean meat
Potato
Salad
Green vegetable
Custard
Fruit or ice cream
Whole wheat bread with butter
Milk or cocoa

BETWEEN MEALS

Egg nog beef juice
Sandwiches of whole wheat bread
Milk drinks
Use honey or molasses instead of sugar throughout

IRRADIATION

Roentgen therapy is of value in the reduction of the excessive number of red blood cells in *polycythemia vera* in the treatment of the *leukemias* and in certain of the disturbances of the lymph glands such as *Hodgkin s disease* and *follicular lymphoblastoma* An experienced roentgen therapist is needed to carry out this form of therapy which necessitates frequent hemograms in order to prevent the therapeutic effect from progressing to the point of causing serious and irreparable damage to bone marrow

The effects of roentgen therapy may be duplicated by oral doses of *radioactive phosphorus* (p 3824) when that preparation can be made available and by nitrogen mustard

TRANSFUSION

Transfusions of whole blood may be carried out by *intravenous* or *intramedullary* routes We can see no advantage to the latter procedure which is technically somewhat more difficult than direct introduction into an accessible vein Transfusion of blood is useful for the restoration of the numbers of the circulating erythrocytes and it may also be employed in the hemorrhagic diathesis for anticoagulant effect

SURGERY

Surgery of the diseases of the blood and blood forming organs is limited almost exclusively to splenectomy Extensive excision of the lymph glands as formerly practiced in Hodgkin s disease is no longer advocated

Splenectomy—Removal of the spleen requires careful preoperative and postoperative precautions as well as meticulous technical considerations Prior to and following splenectomy blood transfusions are usually required The subcutaneous injection of 0.5 cc of 1 1000 epinephrine after the abdomen is opened and just before ligation of the splenic vessels may contract the spleen to half its size thereby forcing large numbers of red cells into the general circulation Particular care is exercised to separate the tail of the pancreas from the splenic hilus lest pancreatic necrosis result In congestive splenomegaly the extensive collateral circulation by way of the vasa brevia to the stomach may necessitate numerous vessel ligations Adhesions of the spleen to the diaphragm and other organs often complicate the operative procedure

Splenic portal and other venous thromboses may occur postoperatively due to excessive increases in the numbers of the platelets Thrombotic accidents are most frequent in congestive splenomegaly and other conditions associated with normal or high initial platelet counts The prophylactic and remedial effects of anti coagulants particularly heparin merit consideration under these circumstances

Absolute indications for splenectomy

1 Chronic familial hemolytic anemia
2 Essential thrombocytopenia

ance of the drug it may require 1 to 2 weeks for the prothrombin time to return to normal

Toxic Manifestations —The use of dicoumarol is attended occasionally by nausea vomiting and lumbar pain hemorrhagic phenomena are common and include *hematuria epistaxis purpura* and *hemorrhage* at the site *of an operative wound* *Repeated blood transfusions* are of little value in arresting hemorrhage induced by dicoumarol but the action of the drug may be somewhat neutralized by 60 mg doses of menadione There is no evidence of any interference with liver function following the use of dicoumarol other than the impairment of prothrombin formation A sudden increase in the blood sedimentation rate is a reliable sign of hemorrhage in a patient receiving dicoumarin

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Adjuvants —In addition to dietary control it is usually wise to use iron salts and vitamin concentrates as supplements

Type Diet

Breakfast

Glass of fruit juice
Stewed or raw fruit
Oatmeal wheatena or any whole grain cereal
Egg
Whole wheat bread with butter
Milk or cocoa

Midday Meal or Supper

Cream soup or vegetable soup
Liver or lean meat
Potato
Salad
Green vegetable
Custard
Fruit or ice cream
Whole wheat bread with butter
Milk or cocoa

CHAPTER 50

CONDITIONS DUE TO DISTURBANCES OF ERYTHROCYTES

THE ANEMIAS

UNDER normal conditions in the adult erythrocytes are produced in the *red bone marrow* of the sternum ribs vertebrae skull and flat bones of the pelvis With abnormal demands hematopoietic function is assumed by

3. Primary splenic granulocytopenia
4. Felty s syndrome
5. Torsion of spleen
6. Rupture of spleen
7. Abscess of spleen
8. Cysts of spleen
9. Tumors of spleen
10. Thrombosis of splenic vein

Occasional indications for splenectomy

1. Congestive splenomegaly (Banti)
2. Huge splenic enlargement in schistosomiasis Gaucher s disease malaria and kala azar
3. Marked neutropenia in Boeck's sarcoid
4. Marked thrombocytopenia in Boeck s sarcoid tuberculosis or Gaucher s disease
5. Acute hemolytic anemia (Lederer) not responding to several blood transfusions
6. Acquired hemolytic anemia not responding to non operative therapy
7. Refractory anemia and hyperplastic bone marrow

Blood Changes after Splenectomy —A conspicuous rise in white blood cells and platelets starts soon after splenectomy These may later fall to normal or even subnormal levels Months later the blood may show target erythrocytes Howell Jolly bodies and increased hypotonic resistance to hemolysis

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UNDER normal conditions in the adult, erythrocytes are produced in the *red bone marrow* of the sternum, ribs, vertebrae, skull and flat bones of the pelvis. With abnormal demands, hematopoietic function is assumed by

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Blood Changes after Splenectomy—A conspicuous rise in white blood cells and platelets starts soon after splenectomy These may later fall to normal or even subnormal levels Months later the blood may show target erythrocytes Howell Jolly bodies and increased hypotonic resistance to *hemolysis*

Iron Deficiency Anemia
Physiological anemia of newborn
Nutritional anemia of infancy
Goat's milk anemia
Chlorosis
Physiological anemia of pregnancy
Hypochromic anemia of pregnancy
Idiopathic hypochromic anemia
Marrow Anemias
Aplastic anemia (hypoplastic aregenerative)
Myelophthisic anemia (leuko-erythroblastic)
Polycythemia
Relative polycythemia
Symptomatic polycythemia
Polycythemia vera

Anemia Due to Bleeding

The simplest types of anemia are due to mechanical blood loss Acute and chronic hemorrhages are frequent and of diverse etiology in clinical practice

Acute Hemorrhage

Acute exsanguination is a dramatic and terrifying clinical emergency Obvious bleedings are observed at sites of injuries or operations non traumatic hemorrhages include *epistaxis* (p 2193) *hematemesis* (p 1764) *melena* (p 1843) *hemoptysis* (p 2058) *metrorrhagia* (p 2565) and *menorrhagia* (p 2557)

Occult bleeding occurs into the pericardium pleura peritoneum and ventricles of the brain In confined spaces the bulk of the extravasated blood increases pressure relations sufficient to accomplish hemostasis

See *Hemopericardium* (p 968) *Hemothorax* (p 2032) *Hemoperitoneum* (p 2657) *Cerebral Hemorrhage* (p 1439) *Intraventricular Hemorrhage* (p 1441) *Subarachnoid Hemorrhage* (p 1445)

Clinical Manifestations —Acute bleeding is often accompanied by shock With *external bleeding* the flow of sanguineous material is the arresting manifestation With *internal bleeding* as exemplified by hemorrhage into the upper bowel the patient develops the symptoms of blood loss or forward circulatory failure He usually becomes restless the pulse rate rises the blood pressure falls the face becomes pale and sweat stands out on the brow *Syncope* may occur and even the inexperienced observer realizes that some dire emergency has arisen In patients with coronary sclerosis an anginal syndrome (p 890) may be evoked due to myocardial anoxia

Laboratory Data —Initially when bleeding is brisk the hemoglobin and red count are unchanged The first hematologic response is a polymorphonuclear leukocytosis With restoration of the blood volume the hemoglobin falls and small numbers of reticulocytes appear Later a hypochromic microcytic anemia is found

Treatment —The urgent therapeutic demands in acute bleeding preclude any laboratory investigations The salient principles of therapy conducted simultaneously consist of attempts at hemostasis the replacement of lost fluid and blood and relief of shock

Hemostasis —Hemostasis is effected by means of pressure packing or actual ligation of bleeding points preferably under anesthesia Accessible

specialized areas in *yellow bone marrow* and *extramedullary hematopoietic centers* particularly liver spleen and lymph nodes

When these usual and unusual responses are inadequate the peripheral blood exhibits manifestation of the disturbance The total red cell volume is decreased coloring matter is diminished and immature or imperfect red cells are found in the peripheral blood These changes are reflected for the practitioner in his laboratory examinations since he finds a low red blood cell count a diminished hemoglobin percentage changes in the color index and the appearance of microcytes macrocytes reticulocytes and nucleated cells of the primitive varieties in the stained spread

Causative Mechanisms

The anemias are produced by several different mechanisms The most obvious cause is blood loss through *hemorrhage* (p 1057) *iron deficiency anemias* (p 1085) result from lack of the element essential for the production of hemoglobin *hyperchromic anemias* (p 1077) with imperfect maturation of the erythrocytes are due to abnormalities involving the erythrocyte maturation factor *hemolytic anemias* (p 1060) follow upon excessive destruction of red cells and the *marrow types* (p 1064) are secondary to atrophy or replacement of erythrogenic centers in bone marrow

Each variety of anemia presents a characteristic clinical syndrome and requires a specific therapeutic approach *Transfusion* and *hemostasis* are the chief factors of therapy when there is mechanical blood loss, *iron* is the therapeutic requirement in the hypochromic anemias due to deficiency *liver extract* and gastric *anti anemic principles* are needed in hyperchromic anemias resulting from failure of proper maturation of red cells removal of the toxic cause for hemolysis may be of curative value in conditions characterized by excessive blood destruction

Anemia Due to Bleeding
- Acute hemorrhage
- Chronic blood loss

Hemolytic Anemia
- Chronic familial hemolytic anemia (familial spherocytosis Chauffard Minkowski)
- Acquired hemolytic anemia (Hayem Widal)
- Symptomatic hemolytic anemia
- Sickle cell anemia (drepanocytic anemia meniscocytosis)
- Erythroblastosis foetalis (icterus gravis neonatorum)
- Target cell anemia (familial microcytic anemia)
- Erythroblastic anemia of Cooley (Mediterranean anemia thalassemia)
- Von Jaksch s anemia
- Acute hemolytic anemia of childhood (Lederer)

Acute Hemoglobinemias and Hemoglobinurias
- Due to transfusion of incompatible blood
- Paroxysmal due to cold
- Nocturnal paroxysmal hemoglobinuria (Marchiafava Michel)
- March hemoglobinuria
- Myoglobinuria
- Blackwater fever
- Acute epidemic hemoglobinuria (Winckel)

Disturbance of Erythrocyte Maturation Factor
- Macrocytic hyperchromic anemia (Addison s Biermer s primary or pernicious anemia)
- Symptomatic hyperchromic anemia

cavities such as the nose and the vagina are packed with gauze a lung is collapsed by *pneumothorax* (p 2034) and bleeding from an extremity is controlled with a *tourniquet*

Replacement of Fluid—While hemostasis is being accomplished preparations are made for replacement of fluid preferably by intravenous infusion The most accessible fluid is employed at first Ordinarily physiological saline and 5 per cent dextrose in saline are infused until blood plasma can be obtained Meanwhile efforts are made to obtain blood from patient and donors for cross agglutination (p 3708) As soon as possible at least a pint of citrated blood is added to the intravenous drip

In acute hemorrhage there is great temptation to replace the lost fluid with excessive rapidity While it is not necessary to adhere to the usua slow rate of 2 to 4 cc per minute not more than 5 to 10 cc should be introduced per minute One of the protective measures in acute hemorrhage is the fall of blood pressure the more rapid rates are apt prematurely to restore the normal level of tension under which circumstance bleeding may be perpetuated or initiated anew The slower rates do not disturb hemodynamics and favor the formation of a firm clot

Relief of Shock—See p 928

Hematinics—Following the restoration of blood volume the patient regenerates lost blood more rapidly if 1 to 2 gm (15 to 30 grains) of ferrous sulfate are given each day Liver extract has no specific value and its administration complicates the regimen

Coagulants—The coagulants (p 1049) are of little value in the treatment of acute hemorrhage *Vitamin K* is worth giving in suspected deficiency states such as hemorrhagic disease of the newborn or obstructive jaundice Local applications of *snake venom* (1 10 000) or *thromboplastin* may be tried particularly in hemophiliacs but systemic injections of *calcium* and *cevitamic acid* hold little promise

CHRONIC BLOOD LOSS

The problem of chronic blood loss differs from that of acute hemorrhage There is no associated shock and the accessory erythrogenic centers are stimulated to aid the normally active red bone marrow

Clinical Manifestations—Chronic bleeding usually occurs from the various body orifices Frequent epistaxis constant vaginal oozing and the continuous passage of changed or fresh blood in the stool constitute the commonest clinical examples It is amazing to note how frequently patients take for granted a prolonged menstrual bleeding and the daily appearance of red blood in toilet bowl or on toilet paper Even the most intelligent fail to realize the ominous implication of a tarry stool (p 1843)

Slow oozing of blood produces remarkably few clinical manifestations The patient may be bled white before complaints are registered The level at which symptoms are initiated varies In acute hemorrhage air hunger appears when the hemoglobin has fallen 30 to 40 per cent while in chronic bleeding patients may carry out a relatively normal existence with figures as low as 40 per cent we have in fact observed instances where the patient continued work with a hemoglobin level of about 20 per cent

The manifestations of chronic anemia are insidious They include

TABLE 71.—DIFFERENTIAL DIAGNOSIS OF PRINCIPAL TYPES OF ANEMIA

	Color Index	Diameter of Red Cells	Jaundice	Hemoglobin in Urine	Urobilin in Urine	Fragility of Cells	Marrow	Response to Iron	Response to Anti Anemia Principle
Acute Hemorrhage	Normal	Unchanged	Variable	None	No	Normal	Hyperplastic	Favorable	No
Chronic Blood Loss	Low	Small	Absent	None	No	Decreased	Hyperplastic	Favorable	No
Hemolytic Anemia	Normal	Small	Marked	None	Marked	Markedly Increased	Hyperplastic (Normoblasts)	No	No
Hemoglobinemias	Normal	Variable	Slight	Marked	Slight	Variable	Hyperplastic	No	No
Disturbances of Erythrocyte Maturation Factor	High	Large	Slight	None	Moderate	Normal	Hyperplastic (Megaloblasts)	No	Specific
Iron Deficiency	Low	Small	Absent	None	No	Normal	Hyperplastic (Normoblasts)	Excellent	No
Marrow Anemias	Normal	Normal	Absent	None	No	Normal	Variable	No	No

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Relief of Shock—See p 998

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The manifestations of chronic anemia are insidious They include

TABLE 72 —DIFFERENTIAL DIAGNOSIS

	Clinical Features	Jaundice	Spleen	Liver
Familial (p 1061)	Congenital chronic with crises	Moderate	Enlarged	Enlarged
Acquired (p 1064)	Not hereditary no etiology	Moderate	Palpable	Normal
Symptomatic (p 1064)	Exposure to infection toxin drug or chemical	Moderate	Palpable	Normal
Sickle cell (p 1065)	Negroes hereditary	Slight	Variable	Palpable
Erythroblastosis foetalis (p 1067)	Newborn see Rh factors in maternal and paternal bloods (p 000)	Extreme	Enlarged	Enlarged
Target cell (p 1071)	Mediterraneans adults	Moderate	Enlarged	Enlarged
Cooley s (p 1071)	Mediterraneans infants	Moderate	Enlarged	Enlarged
Lederer s (p 1073)	Children	Moderate	Palpable	Normal

fatigue impaired concentration giddiness tinnitus roaring in the head light headedness visual disturbances tachycardia dyspnea anorexia faintness and syncope Examination reveals the obvious pallor whiteness of the sclerotics *tachycardia and hemic cardiac murmurs*

Differential Diagnosis —See *Anemia* (p 1058)

Laboratory Data —A low *color index* is the characteristic blood finding in chronic hemorrhage The hemoglobin may be between 20 and 40 per cent while the red blood count is as high as 3 000 000 In the stained smear microcytosis hypochromia anisocytosis and poikilocytosis are observed The leukocytes and thrombocytes are normal nucleated red blood cells are not usually present

When the source of bleeding is not clinically obvious several *stools* are examined for the presence of occult blood and intestinal parasites (p 1893) the *coagulation tests* are made to ascertain the possible presence of a hemorrhagic diathesis (p 1108)

Treatment —The generic treatment of chronic blood loss does not differ from that of acute hemorrhage The initial efforts are aimed at the accomplishment of *hemostasis* (p 1057) Meantime lost blood is replaced by *transfusion* a diet rich in *iron* (p 682) is prescribed together with daily doses of 1 to 2 gm (15 to 30 grains) of *ferrous sulfate* Efforts are made to correct any existent tendency toward hemorrhage (p 1108) Cevitamic acid and menadione are given if there are evidences of vitamin C (p 627) or K deficiency (p 630)

THE HEMOLYTIC ANEMIAS

The hemolytic anemias result from abnormal hemolysis or the acceleration of the normal tempo of red cell destruction Some hemolytic processes are acute and others are chronic a few arise from obvious etiologic factors a diminishing number are idiopathic The chemical and metabolic

OF THE HEMOLYTIC ANEMIAS

Leg Ulcers	Lymph Nodes	Fragility	Unstained Blood	Stained Spread	Splenectomy
Present	Normal	Increased	Marked spherocytosis	Microcytes	Curative
Absent	Normal	Slightly increased	Slight spherocytosis	Macrocytes	May be tried
Absent	Normal	Normal	Normal	Microcytes	May be tried
Present	Enlarged	Decreased	Marked sickling	Target cells	Contraindicated
Absent	Normal	Normal	Normal	Erythroblasts	Contraindicated
Absent	Normal	Decreased	Slight sickling	Target cells	Contraindicated
Absent	Normal	Decreased	Slight sickling	Target cells	Contraindicated
Absent	Normal	Increased	Normal	Erythroblasts	May be tried

changes referable to the hemolytic process are fully described in the section on *jaundice* (p 1951)

CHRONIC FAMILIAL HEMOLYTIC ANEMIA (FAMILIAL SPHEROCYTOSIS CHAUFFARD MINKOWSKI S DISEASE)

Chronic familial hemolytic anemia is a hereditary disease of varying severity It may be observed in infancy or childhood but often does not make its appearance until late in adult life The most significant abnormalities are the simultaneous occurrence of *spherocytosis splenomegaly* and *increased fragility of the red blood cells* The blood characteristics are *transmitted as* dominant hereditary factors They usually are found to some degree in other members of the patient s family who suffer mild or asymptomatic forms of the disease

Clinical Manifestations—The completely developed syndrome of hemolytic jaundice combines the features of *chronic anemia* with acute episodes or *hemolytic crises* The patient gives a long history of yellow discoloration of skin and sclerae lack of energy easy fatigability tachycardia and dyspnea *on exertion* Interspersed with these chronic symptoms are manifestations of an acute illness with fever and severe *abdominal pain* The exacerbations are accompanied by accentuated hemolysis the chronic symptoms become more severe when the crisis has subsided

The distinguishing features on physical examination are the presence of *jaundice* (p 1951) *splenomegaly* (p 1129) and slight *hepatomegaly* (p 1973) The spleen varies in size and is usually larger during a hemolytic crisis Rarely it *is not palpable at all but most often it is* approximately three fingers below the costal margin and may be felt as far down as the level of the umbilicus Indolent *leg ulcers* are sometimes encountered

Depending upon the degree of anemia *hemic cardiac murmurs* (p 973) are present They often give rise to diagnostic difficulty since they sug

gest the possibility that the disease is initially an *endocarditis* with a secondary splenic enlargement as seen in subacute bacterial endocarditis

Laboratory Data.—The diagnosis of hemolytic anemia is suggested strongly by the hemogram it is proved definitively by the reactions to hypotonic saline solution

The Hemogram—The hemoglobin and erythrocyte counts vary considerably depending upon the course of the disease Most often there is a moderate *anemia* with the coloring matter in the vicinity of 60 per cent and the red cells approximating 3 000 000 After a hemolytic crisis the count may fall to 1 000 000 but the numbers approach the normal in a

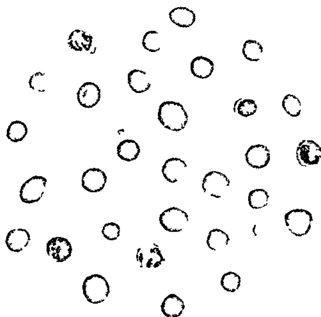


Fig 230—Familial hemolytic anemia (Cresyl blue stain used to show the reticulocytes followed by Wright's stain)*

phase of recession The white cells and platelets reveal no constant changes except during crises when both are increased

The stained spread reveals a *microcytosis* the cells being well filled with hemoglobin In the unstained preparation the phenomenon of *spherocytosis* is observed the normally biconcave erythrocyte is globular and thickened Evidences of strain on the marrow are afforded by the appearance of large numbers of *reticulocytes* and of *polychromatophilia* Less frequently nucleated forms are found in the peripheral blood

Increased Fragility—The characteristic feature of the disease is increased osmotic fragility of the red blood cells Hemolysis may start in 0 8 per cent and be complete in 0 4 per cent of salt solution (p 3706)

Evidences of Increased Hemolysis—Evidence of *increased bilirubin pro*

* Murphy Anemia in Practice

duction is afforded by increased urinary and fecal urobilinogen elevation of the icterus index of the blood serum and hyperbilirubinemia The qualitative van den Bergh reaction is positive in the indirect test (p 1047) *Bilirubinuria* does not occur the *stools* are normally colored or even darker than normal as opposed to the findings in obstructive jaundice False positive serological tests for *syphilis* (p 331) may be encountered in this disease as in any hemolytic syndrome The bone marrow shows a marked increase in *erythroblasts* and *normoblasts* (p 1043)

Diagnosis—The diagnosis of hemolytic jaundice offers no difficulty when findings and course are typical In the chronic phase the features of an *obstructive jaundice* (p 1051) are simulated but bile pigments continue to be present in feces and absent from urine The long history of discoloration the finding of similar conditions in other members of the family and the comparative well being of the patient argue strongly against the presence of an anatomical lesion of sufficient severity to produce biliary obstruction

During the *crises* the combination of abdominal pain fever and hemic murmurs suggests an acute or subacute *endocarditis* This fear is allayed only by the sterility of the blood culture In other instances the presence of pigmentation fever and abdominal pain suggests organic disease of the *gallbladder* (p 1093) Since the excessive metabolism of bile pigment in hemolytic jaundice often results in a secondary cholelithiasis the clinician must decide whether the systemic disturbances result from a hemolytic crisis in a patient whose jaundice is complicated by gallstones or whether the febrile process is due to a cholecystitis in a patient who has also a hemolytic icterus In the former situation repeated blood counts reveal progressively lower figures for hemoglobin and erythrocytes whereas cholecystitis is accompanied by an increasing *leukocytosis* (p 1096)

The differentiation of *hemolytic* and the *infectious* types of jaundice is more completely considered in the section on *jaundice* (p 1951) The features of the types of hemolytic jaundice are charted elsewhere (p 1060)

Course and Prognosis—The course of hemolytic icterus is one of chronicity Sooner or later manifestations of anemia develop and a hemolytic crisis is encountered The disease may remain dormant for years but spontaneous recovery does not take place Indeed if the patient does not receive treatment he will certainly be invalided and may succumb at any time

Treatment—The specific treatment of hemolytic icterus requires *removal of the spleen* (p 1053) The operative procedure in the majority of instances is exceedingly effective Splenectomy almost always terminates the excessive hemolysis of the red cells but the spherocytosis and abnormal saline fragility are permanent After operation there are fairly rapid increases in hemoglobin content and red blood-cell counts with a fall in reticulocyte counts The jaundice usually disappears as soon as the hemolytic process has ended

Splenectomy is deferred in the midst of a crisis and is performed preferably when the condition is quiescent If a patient in crisis is not improved by four or five transfusions splenectomy may become mandatory despite a low blood count Before the operation is undertaken the anemia is corrected by *multiple transfusions* until the red blood count approaches

4 000 000 and the hemoglobin exceeds 80 per cent In the conduct of blood transfusion the expert hematologist is consulted since many patients who suffer from this disease are intolerant to transfused blood determination of the *Rh status* (p 1067) of the patient s blood is important if trouble is to be avoided Even when all precautions are exercised post transfusion hemolytic reactions are encountered

Alternatives to splenectomy are *roentgen therapy to the spleen* and the simpler surgical procedure of *ligation of the splenic artery* Neither of *these is recommended since* the results are not consistent or comparable to those obtained by the complete removal of the spleen The use of *hematinics* or *liver extracts* holds no promise

In those patients who fail to respond to splenectomy the hemolytic process may be perpetuated by residual or accessory splenic tissue or by *the reticulo endothelial system*

ACQUIRED HEMOLYTIC ANEMIA (HAYEM WIDAL)

An acquired or atypical hemolytic anemia is occasionally encountered The principal features are those of the congenital variety (p 1061) but all *manner of variants confuse the clinical manifestations*

Clinical Manifestations—The history of hereditary transmission is lacking in acquired hemolytic anemia Similar disturbances are not found in other members of the family enlargement of the spleen may not be demonstrable spherocytosis and increased fragility of the red cells may be difficult of demonstration In some instances the red cells are macrocytic or pseudomacrocytic due to the presence of many reticulocytes which are larger than the adult cell

The consistently positive findings include evidences of severe hemolysis jaundice and occasional hemoglobinemia and hemoglobinuria Cold hemagglutinins (auto agglutinins) and autolysins may be demonstrable in the plasma, a thrombocytopenia may be present

Treatment—If there are no evidences of activating causes such as are described in symptomatic types (p 1065) the management of these patients presents a serious problem *Blood transfusions* are of value only insofar as they tide the patient over a hemolytic episode *Splenectomy* (p *1053) is considered* when the symptoms warrant but the results are not so consistent and striking as the effects noted in the typical familial varieties of this disturbance

SECONDARY OR SYMPTOMATIC HEMOLYTIC ANEMIA

Hemolytic anemia may arise as the result of a variety of tangible etiologic agencies The *infectious causes* include streptococcal or Welch bacillus septicemias malaria Bartonella invasions and the congenital syphilis of early infancy The *toxic substances* which produce hemolytic anemia are industrial exposure to lead (p 762), hydrogen sulfide (p 749) or nitrobenzol (p 757) Sensitivity to the fava bean (favism) may manifest itself as a hemolytic anemia *and in sensitive individuals hemolysis may* be produced by administration of *sulfonamides* (p 88) *phenylhydrazine* (p 1094) and the *nitrobenzols* (p 757) Symptomatic hemolytic anemia occasionally occurs as a complication of leukemia follicular lymphoblastoma Hodgkin's disease cirrhosis of the liver and carcinomatosis The

differentiation of symptomatic and other varieties of hemolytic anemia is charted elsewhere (p 1060)

From Lead—The hemolytic anemia of lead poisoning is usually of the chronic variety Lead apparently acts directly on the envelope of the red cell rendering it less elastic The blood reveals a large increase in the stippled cells and there is characteristic basophilic degeneration more completely described elsewhere (p 764) Therapy requires discontinuance of exposure to the metal

From Sulfonamides—The administration of *sulfonamides* (p 88) gives rise to two types of hemolytic anemia These represent toxic manifestations in sensitive individuals An *acute hemolytic anemia* may occur after the first few doses as an obvious idiosyncrasy which cannot be predicted or prevented the clinical and hematological findings are identical with those of a severe hemolytic process The long continued use of the drug may produce a *slowly progressive anemia* probably due to the combination of excessive hemolysis and bone marrow inhibition (p 1043)

Treatment involves cessation of the drug and supportive transfusions

SICKLE CELL ANEMIA (DREPANOCYTIC ANEMIA MENISCOCYTOSIS)

Sickle cell anemia is a chronic recurring hereditary hemolytic anemia dependent upon a congenital defect in the structure of the erythrocytes The disease is almost restricted to the Negro although a few examples have been described in persons from Mediterranean regions Sickle cell anemia is seen most often in childhood but may make its first appearance in infancy Since the tendency of this disease is towards improvement severe examples in adult life are not common

Asymptomatic Sicklemia—Asymptomatic sicklemia without evidence of hemolysis and anemia is present in about 7 per cent of Negroes in the United States The trait is often discovered in the parents or relatives of patients who have frank sickle cell anemia

Clinical Manifestations—The symptoms of meniscocytosis are varied and insidious The mother may bring her youngster to the physician because the child has been ailing for some time The child exhibits lack of vitality easy fatigability an icteric tinge to the sclera loss of appetite dyspnea tachycardia hemic cardiac murmurs episodes of abdominal or extremity pain and indolent leg ulcers On other occasions the child is seen because of the presence of an unrelated infection and the anemia is observed as a chance finding

Exacerbations of sickle cell anemia occur in association with infection At these times there may be the symptoms of an *acute abdominal disturbance* (p 2730) due to perisplenitis and multiple splenic infarcts The attack is initiated by the sudden onset of diffuse abdominal pain with localization in the left upper quadrant Distention and tenderness are associated with nausea vomiting and fever Inquiry may reveal the previous occurrence of similar episodes

The clinical manifestations may resemble those of *rheumatic fever* with endocarditis and polyarthritis There may be dyspnea enlargement of the heart hemic cardiac murmurs and hepatomegaly Some patients exhibit evidences of *cerebral dysfunction* with convulsive disorders twitchings and paralyses resulting from vascular thrombosis

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course required At the termination of the hemolytic episode the rise in red blood cells is likely to be very rapid

ERYTHROBLASTOSIS FOFTALIS (ICTERUS GRAVIS NFONATORUM)

Erythroblastosis foetalis is a hemolytic syndrome of late intra uterine and early extra uterine life It bears a close relationship to congenital hydrops foetalis certain types of stillbirth neonatal deaths the congenital anemias of the newborn and transfusion reactions in pregnancy

Pathogenesis—Erythroblastosis foetalis results from a hemolytic process initiated by an antigenic *Rh factor* in the red cells of humans and Macacus rhesus monkeys

In order to understand the complexities of the clinical syndrome the practitioner must be familiar with the terms defined below (Wiener A S J.A.M.A 1945 *127* 294)

Anti rhesus serums Immune serums prepared in rabbits guinea pigs goats and other animals by injecting them with the blood of rhesus monkeys

Anti Rh human serums Human serums (usually obtained from mothers of erythroblastic infants) which gave reactions paralleling the anti rhesus serums also known as standard anti Rh serums

Rh sensit at on The act of becoming sensitive to the Rh factor This may occur in one of two ways namely as a result of a transfus on of Rh positi e blood or as the result of pregnancy with an Rh positive fetus Natu al sens tivity to the Rh factor does not occur and only 1 in 25 to 50 Rh negati e persons exposed to the Rh antigen by transfus on or pregnancy becomes sensitized Rh factors three in number are designated as Rh_0 *Rh* and *Rh* respectively

Rh aggl tin ns The animal anti rhesus agglut n ns are all of the same spe ific ty (8 per cent pos ti e in white persons) The anti Rh agglutinins of human serums have three d fferent spec ficities corresponding to the three Rh factors namely *Anti* Rh_0 (85 pe cent posi tive in white persons) *anti Rh* (0 per cent positive) and *anti Rh* (30 per cent posi tive)

Rh agglutinogens The Rh antigens are Rh_1 (or Rh_0) *Rh* (or Rl)) *Rh* *Rh* and Rh_0

Rh ant serums Antiserums reacting with one or more of the Rh factors Among human be gs in ad i t on to serums conta ing only one sort of Rh agglutin n there are some with two Rh agglutinins Five common varieties of human Rh ant serums are *a t* Rh_0 *a ti Rh* *anti Rh* *ant* Rh_0 (containing two agglutinins anti Rh_0 and ant Rh) and *ant* Rh_0''

Rh blood types Tests with anti Rh_0 anti Rh and anti Rh yiel i e ght standard types The names of these types and their approximate frequenc s among white persons in New York City are as follows type Rh_1Rh 13 per cent Rh_1 54 5 pe cent *Rh* 15 pe cent Rh_0 2.5 per cent *Rh Rh* 1 in about 10 000 *Rh* 1 0 per cent *Rh* 0 3 per cent an l *Rh*— 13.5 per cent The e are striking d ffere ces in the d stribution among different races for example in Negroes type Rh_0 exceeds 40 per cent i Mongolian race Rh— is v rtually absent and so on

Hr fa tor The factor present in the agglutinogens determin d by genes *rh* Rh_0 *Rh* and Rh_2 Hence only persons belonging to type Rh_1 (prov ded they belon to genotype Rh_1Rh_1 or Rh_1Rh) or type Rh (rare genotype *Rh Rh*) can poss bly be Hr ne at ve Pers ns belong g to any of the other six Rh blood types are uniformly Hr positive The common idea that infants with hemolytic d sease du to the Hr factor are always Rh neg tive is wrong su h infants must in fact always be Rh po t e

Anti H serum Serum apable of react n with blood contain ng the Hr fa tor

Physical examination reveals pallor of the conjunctiva The icterus may be difficult to recognize because of the negroid pigmentation Rapid heart action cardiac murmurs and cardiac enlargement occur The *liver* may be palpable the *spleen* may be normal or enlarged to four fingers below the costal margin A mild generalized *lymphadenopathy* is of frequent occurrence

Hemogram—Examination of the peripheral blood reveals a *normochromic anemia of varying severity Bone marrow hyperactivity* is suggested by the presence of 5 to 20 per cent reticulocytes polychromatophilia nucleated red blood cells a mild leukocytosis with a shift to the left and a slight increase in blood platelets

The stained red blood cells show a *moderate macrocytosis* and large numbers of *target cells* The latter are erythrocytes containing a central spot of hemoglobin separated by a clear zone from a rim of hemoglobin about the edge *Sickle cells* are not usually seen on the stained dry smear They are best demonstrated by placing a drop of blood under a coverslip whose edges are rimmed with petrolatum to exclude air from the preparation In a variable period of time the red cells assume bizarre crescentic shapes with long filamentous processes extending from the tips of the crescents Other cells in which crenation and sickling are occurring together appear as holly leaves When hemolysis is active the sickle phenomenon appears in one hour at room temperature When the sickling is latent it may take as long as twenty four hours before the abnormality is fully developed The sickling is due to anoxemia and increase in acidity of the medium A number of erythrocytes circulate as sickle forms on the *venous side of the circulation but revert to normal shape when the blood* is oxygenated in the lungs See Fig 227

During the period of hemolysis the *icterus index* is elevated a marked fecal and urinary excretion of *urobilinogen* is present the *van den Bergh reaction* is indirect and bile pigments are absent from the urine The *osmotic fragility* of the red cells to hypotonic saline is decreased Roentgen examinations of the skull and long bones in a longstanding sickle cell anemia are likely to reveal changes similar to but not as marked as those in Cooley s erythroblastic anemia (p 1071)

Diagnosis—The difficulties in the differential diagnosis of sickle cell anemia have been previously indicated Splenic infarction and perisplenitis produce an *acute abdominal syndrome* suggesting a surgical lesion (p 3555) The hemic murmurs pains in the extremities and fever simulate the *rheumatic syndrome* (p 186) Icterus and anemia constitute a symptom complex of many *hemolytic diseases* (p 1060)

From clinical data alone a definite diagnosis cannot be established In the presence of any suspicion of sickling the blood must be examined in every colored child If sickling is demonstrable the secondary problem is the evaluation of symptoms since rheumatic fever and abdominal syndromes of a surgical nature occur in these patients as well as in those with normal blood

Treatment—Treatment of sickle cell anemia is ineffective *Splenectomy* (p 1053) is a dangerous and difficult technical procedure and is without effect on the sickling phenomena or upon the tendency to crisis Supportive and general hygienic measures and protection from infection are of

course required At the termination of the hemolytic episode the rise in red blood cells is likely to be very rapid

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Rh sensitization The act of becoming sensitive to the Rh factor This may occur in one of two ways namely as a result of a transfusion of Rh positive blood or as the result of pregnancy with an Rh positive fetus Natural sensitivity to the Rh factor does not occur and only 1 in 25 to 50 Rh negative persons exposed to the Rh antigen by transfusion or pregnancy becomes sensitized Rh factors three in number are designated as Rh_0 *Rh* and *Rh* respectively

Rh agglutinins The animal anti rhesus agglutinins are all of the same specificity (8 per cent positive in white persons) The anti Rh agglutinins of human serums have three different specificities corresponding to the three Rh factors namely *Anti* Rh_0 (85 per cent positive in white persons) anti *Rh* (70 per cent positive) and anti *Rh* (30 per cent positive)

Rh agglutinogens The Rh antigens are Rh_1 (or Rh_0) *Rh* (or Rh_0) *Rh* *Rh* and Rh_0

Rh antiserums Antiserums reacting with one or more of the Rh factors Among human beings in addition to serums containing only one sort of Rh agglutinin there are some with two Rh agglutinins Five common varieties of human Rh antiserums are *anti* Rh_0 *anti Rh* *anti Rh* *anti* Rh_0 (containing two agglutinins anti Rh_0 and anti Rh) and *anti* Rh_0

Rh blood types Tests with anti Rh_0 anti Rh and anti Rh" yield eight standard types The names of these types and their approximate frequencies among white persons in New York City are as follows type Rh_1Rh 13 per cent Rh_1 54.5 per cent *Rh* 15 per cent Rh_0 2.5 per cent *Rh Rh* 1 in about 10 000 *Rh* 1° per cent *Rh* 0 3 per cent and *Rh*— 13 5 per cent There are striking differences in the distribution among different races for example in Negroes type Rh_0 exceeds 40 per cent in Mongolian races Rh— is virtually absent and so on

Hr factor The factor present in the agglutinogens determined by genes *rh* Rh_0 *Rh"* and Rh_2 Hence only persons belonging to type Rh_1 (provided they belong to genotype Rh_1Rh_1 or Rh_1Rh') or type Rh (rare genotype *Rh Rh*) can possibly be Hr negative Persons belonging to any of the other six Rh blood types are uniformly Hr positive The common idea that infants with hemolytic disease due to the Hr factor are always Rh negative is wrong such infants must in fact always be Rh positive

Anti Hr serum Serum capable of reacting with blood containing the Hr facto

Physical examination reveals pallor of the conjunctiva The icterus may be difficult to recognize because of the negroid pigmentation Rapid heart action cardiac murmurs and cardiac enlargement occur The *liver* may be palpable *the spleen may be normal or enlarged to four fingers* below the costal margin A mild generalized *lymphadenopathy* is of frequent occurrence

Hemogram —Examination of the peripheral blood reveals a *normochromic anemia* of varying severity *Bone marrow hyperactivity* is suggested by the presence of 5 to 20 per cent reticulocytes polychromatophilia nucleated red blood cells a mild leukocytosis with a shift to the left and a slight increase in blood platelets

The stained red blood cells show *a moderate macrocytosis and large* numbers of *target cells* The latter are erythrocytes containing a central spot of hemoglobin separated by a clear zone from a rim of hemoglobin about the edge *Sickle cells* are not usually seen on the stained dry smear They are best demonstrated by placing a drop of blood under a coverslip whose edges are rimmed with petrolatum to exclude air from the preparation In a variable period of time the red cells assume bizarre crescentic shapes with long filamentous processes extending from the tips of the crescents Other cells in which crenation and sickling are occurring together appear as holly leaves When hemolysis is active the sickle phenomenon appears in one hour at room temperature When the sickling is latent it may take as long as twenty four hours before the abnormality is fully developed The sickling is due to anoxemia and increase in acidity of the medium A number of erythrocytes circulate as sickle forms on the venous side of the circulation but revert to normal shape when the blood is oxygenated in the lungs See Fig 227

During the period of hemolysis the *icterus index* is elevated a marked fecal and urinary excretion of *urobilinogen* is present the *van den Bergh reaction* is indirect and bile pigments are absent from the urine The *osmotic fragility* of the red cells to hypotonic saline is decreased Roentgen examinations of the skull and long bones in a longstanding sickle cell anemia *are likely to reveal changes similar to but not as marked* as those in Cooley s erythroblastic anemia (p 1071)

Diagnosis —The difficulties in the differential diagnosis of sickle cell anemia have been previously indicated Splenic infarction and perisplenitis produce an *acute abdominal syndrome* suggesting a surgical lesion (p 3555) The hemic murmurs pains in the extremities and fever simulate the *rheumatic syndrome* (p 186) Icterus and anemia constitute a symptom complex of many *hemolytic diseases* (p 1060)

From clinical data alone a definite diagnosis cannot be established In the presence of any suspicion of sickling *the blood must be examined* in every colored child If sickling is demonstrable the secondary problem is the evaluation of symptoms since rheumatic fever and abdominal syndromes of a surgical nature occur in these patients as well as in those with normal blood

Treatment —Treatment of sickle cell anemia is ineffective *Splenectomy* (p 1053) is a dangerous and difficult technical procedure and is without effect on the sickling phenomena or upon the tendency to crisis Supportive *and* general hygienic measures and protection from infection are of

impaired and the disorder attains its greatest severity in utero a *generalized edema* is the outstanding sign of the disease The condition is associated with the development of a *hydramnios* At birth which usually occurs prematurely amniotic fluid and vernix caseosa are stained a deep orange by bile pigment The placenta is large and swollen and the fetus is edematous and pale The skin does not appear icteric but the scleras and the effusions in the serous cavities are bile stained liver and spleen are markedly enlarged If the infant is born alive it fails to survive for more than a few hours

Congenital Anemia of the Newborn—In infants in whom the hemolytic phase has terminated prior to delivery the dominant feature is a *severe anemia* which is present at birth or develops several days later



Fig 231—Infant showing the edema characteristic of the hydropic form of erythroblastosis foetalis

The pallor is intense but jaundice and manifest edema are absent although the liver and spleen remain enlarged Since the operating process has abated before birth the prognosis is considerably more hopeful

Erythroblastosis Foetalis—When the hemolytic process begins late in fetal life and reaches its height at or following birth the child is deeply *icteric* and may become increasingly so during the first week of life At delivery vernix caseosa and amniotic fluid are stained a deep orange The fetus may be born dead or if alive it is feeble and jaundiced The placenta is usually pale and edematous

If the child lives a few days the jaundice deepens and a progressive *anemia* becomes apparent *petechial hemorrhages ecchymoses* and prolonged bleeding time are encountered There is usually an accompanying

Rh incompatibility Incompatibility based on difference with respect to one or more of the Rh factors

Hr incompatibility Incompatibility with respect to the Hr factor

Rh blocking serum (antibody) A serum capable of reacting with blood containing the Rh factor but without producing agglutination though blocking the action of subsequently added anti Rh serums i e Rh positive blood treated with Rh blocking serum can no longer be agglutinated by anti Rh serum To date blocking antibodies of only one specificity have been found namely anti Rho

The Rh factor is present in the erythrocytes of about 85 per cent of the white population regardless of sex Those who possess the factor are known as Rh positive individuals those in whom the factor is absent are labeled Rh negative The Rh factor is inherited from the father as a *simple mendelian dominant* The child born of an Rh positive father and an Rh negative mother may itself be Rh positive When this occurs the Rh factor from the fetus may cross the placental barrier and immunize the Rh negative mother to such an extent that maternal antibodies are formed against the Rh factor These are capable of producing profound changes in mother and child

Maternal Consequences of Rh Immunization—The maternal consequences of the presence of the antibodies are not revealed unless it becomes necessary to perform a blood transfusion using an Rh positive donor Under these circumstances *post transfusion reactions* occur despite the fact that the bloods are compatible according to tests by the slide method Additionally those women in whom transfusion reactions are encountered have a high incidence of *spontaneous abortion stillbirths* and *neonatal deaths* probably as the result of a similar mechanism

Fetal Consequences of Rh Immunization—The Rh factor is capable of injury to the fetus When the anti Rh substances cross the placenta from mother to fetus they combine with the Rh factor of the fetal red blood cells If capillary permeability is impaired the child develops *congenital hydrops foetalis* (Fig 231) When the edema and icterus are relatively minimal a state of *congenital anemia of the newborn* exists The more severe and dramatic manifestations result from the production of severe hemolysis which in the underdeveloped and immature hematopoietic system of infancy becomes manifest as a marked *erythroblastosis* (p 1070) similar to that observed in congenital syphilis and bacterial sepsis of the newborn

Pathology—The outstanding anatomical feature is the presence of large collections of *extramedullary hematopoietic tissue* in the liver spleen kidneys lymph nodes and skin Every tissue in the body has been found to be involved Excessive blood destruction is evidenced by widespread *hemosiderosis* and *bile staining* of the tissues The basal ganglia are often deeply icteric (*kernicterus*) *The bone marrow shows a marked hyperplasia* affecting all cellular elements The placenta is usually two or three times its normal size and edematous with numerous erythroblastic foci

Clinical Manifestations—The clinical manifestations of erythroblastosis foetalis are variable and depend for the most part upon the severity of the reaction and *its relationship* to parturition

Congenital Hydrops Foetalis—When capillary permeability is most

above 60 or 70 per cent An attempt is made to use a donor who is *Rh negative* as well as a member of the same *blood group* as the child However if this is not feasible *group O Rh negative blood* is employed Under no circumstances must the mother s blood be used regardless of tests for compatibility In desperation Rh positive blood of the proper group may be given or the mother s erythrocytes may be washed several times with isotonic salt solution until free of plasma and given resuspended in saline The cord may be used for the initial transfusion

The hemoglobin and red counts are watched carefully from day to day If the child can be tided over the first week or two the subsequent course may be quite uneventful the recurrence of anemia and hemolysis need not be feared although the condition may remain static for several weeks The residual neurological changes persist since they are due to permanent damage of nerve tissue

Future Pregnancies—After the fate of the child has been determined the advisability of further pregnancies is discussed with the parents The woman who has had her first experience with erythroblastosis foetalis is entitled to another trial provided she understands that she faces a possible repetition If there have been repeated unsuccessful pregnancies there is very little possibility that the next child will be normal if conception occurs with the same father The woman who has had several previous successful pregnancies presents a more favorable outlook especially if one or more of the living children is Rh negative

Women who are desperate for progeny may be told of the possibility of *artificial insemination* (p 2508) from an Rh negative donor with the additional precaution of premature induction of labor

TARGET CELL ANEMIA

Several varieties of familial anemia have in common the presence of target and oval shaped red blood cells The most severe of these disturbances is *Cooley s erythroblastic anemia* (p 1071) but other varieties are encountered in adolescents or adults of the Mediterranean areas

Clinical Manifestations—Target cell anemia also known as the adult anerythroblastic form of Cooley s anemia is characterized by *splenomegaly hypochromic anemia* slight *reticulocytosis jaundice* and *bone changes* It occurs in adolescents and adults who live in the region of the Mediterranean Sea

There are wide variations in the clinical features The red blood count may be normal or even increased The splenic enlargement usually is the most prominent feature but some patients show predominant bone changes The pathognomonic features present in all varieties include the presence of oval cells target cells and decreased fragility of the erythrocytes in hypotonic saline solution (p 3706)

Treatment—There is no known form of effective therapy The anemia even though it is hypochromic is not benefited by the administration of iron

ERYTHROBLASTIC ANEMIA OF COOLEY (MEDITERRANEAN ANEMIA THALASSEMIA)

The erythroblastic anemia of Cooley is peculiar to infancy and early childhood It probably is closely related to the adult and adolescent types

edema of the face and extremities, *liver* and *spleen* are enlarged Later there are evidences of irritability of the central nervous system with twitching and convulsions or lethargy Often there is intractable vomiting and diarrhea with a tendency to hemorrhage Surviving children may present evidences of permanent injury to the central nervous system such as *mental deficiency blindness deafness* and *cerebral diplegia* In these the jaundice tends to fade after two or three weeks and is supplanted by a severe anemia which gradually improves

Laboratory Data —Examination of the peripheral blood reveals the *characteristic findings of the disease In the first two days of life* there are normally not more than 2000 nucleated erythroid elements such as normoblasts and erythroblasts per cu mm In erythroblastosis foetalis the number may exceed 100 000 The red blood count varies and is subject to daily decreases of *as many as a million red blood cells per cu mm* The hemoglobin percentage is reduced proportionately Stained smears of the peripheral blood reveal evidences of marked regeneration in addition to the tremendous increase in the *erythroblasts Nuclear fragments* of all kinds are observed and *reticulocytosis* is marked Often the individual cell is larger than normal A *leukocytosis* of 30 000 white blood cells with a shift to the left is a usual finding The *platelets* are variable and may be normal slightly increased or reduced The *bone marrow* shows a marked increase in *normoblasts* and *erythroblasts* See Fig 227

Fragility tests of the red cells reveal an increased span of resistance bleeding and coagulation times are prolonged the icterus index is high and varies with the degree of hemolysis urobilinogen excretion is increased during hemolysis but often the stools are clay colored indicating an obstructive factor in the production of the jaundice the urine may or may not contain bile pigments

Diagnosis —Erythroblastosis foetalis may be confused with other types of *hemolytic anemia* (p 1060) *icterus neonatorum* (p 2761) *biliary obstruction* (p 1951) or *sepsis* (p 2786) In icterus of the newborn jaundice appears on or about the third day of life and is not associated with anemia or splenomegaly In congenital obliteration of the bile ducts acholic stools are observed Sepsis and congenital syphilis are accompanied by *positive blood findings*

The diagnosis of erythroblastosis foetalis usually depends upon the *examination of maternal and paternal bloods* in addition to the investigation of the afflicted child The combination of an Rh negative mother an Rh positive father an Rh positive infant and infantile erythroblastosis is sufficient evidence upon which to establish the diagnosis However since antigens other than the Rh factor are capable of inducing similar changes the tests may be negative

Course and Prognosis —The course and prognosis depend upon the initial severity of the condition and the effectiveness of treatment Infants born with considerable edema rarely survive more than a few hours With marked jaundice at birth and a considerable anemia already present the prognosis is unfavorable

Treatment —Using *exsanguination transfusion* blood is removed by cannulating the radial artery while Rh negative blood is infused in a vein As much as 300 cc may be employed (10 cc per pound) to keep the hemoglobin level

above 60 or 70 per cent *An attempt is made to use a donor who is Rh negative* as well as a member of the same *blood group* as the child However if this is not feasible *group O Rh negative blood* is employed Under no circumstances must the mother's blood be used regardless of tests for compatibility In desperation Rh positive blood of the proper group may be given or the mother's erythrocytes may be washed several times with isotonic salt solution until free of plasma and given resuspended in saline The cord may be used for the initial transfusion

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of target cell anemia As in these latter the condition occurs with rare exceptions in races residing on the northern shore of the Mediterranean and is especially frequent in Sicilians Although there is an evident familial tendency there is no known instance in which the patient has survived the disease and lived to bear children The bloods of the parents of the affected child may show the changes of a target cell syndrome The present opinion concerning the pathogenesis of the disease is that of a disordered hematopoiesis with the production of cells that are hemolyzed more rapidly than normally

Clinical Manifestations —The disease starts in the first year of life but is usually not diagnosed until the middle of the second year Some cases of slow progression and longer duration may first be observed in the fifth year The history is characterized by complaints of *pallor listlessness poor appetite stunting of growth* and *enlargement of the abdomen*

Physical examination is likely to reveal a mongoloid facies and a muddy pallid skin Enlargement of the heart and hemic murmurs are common The abdomen is protuberant because of the markedly enlarged spleen Hepatomegaly also occurs a low grade icterus may be present

Hemogram —Examination of the peripheral blood reveals a severe *hypochromic anemia* There is often a striking *macrocytosis* marked *anisocytosis* and *poikilocytosis* Macrocytic hypochromic red blood cells are more frequent than in any other condition The hemoglobin may be disposed in a very irregular fashion in the red cells *Erythroblasts* and *target cells* are seen in large numbers especially after splenectomy *oval cells* may be a feature The leukocytes are often increased and the platelets approximate the normal In the terminal stages young forms may disappear from the peripheral blood The fragility of the red blood cells to hypotonic saline is abnormal beginning hemolysis may be observed in 0 54 per cent but may not be complete even in distilled water

Laboratory Data —The *icterus index* is usually slightly increased The *van den Bergh reaction* is indirect The *excretion of urobilinogen* in urine and stool is increased but bilirubinuria does not occur The blood calcium and phosphorus levels are normal

The *bone marrow* is extremely *hyperactive* The erythroid *hyperplasia* is to a large degree of a megaloblastic nature resembling that seen in pernicious anemia in relapse Red marrow is present throughout all the bones of the skeleton Resorption of bony structure occurs frequently and occasionally the marrow may actually grow through the bone

Roentgenograms —The roentgenologic picture of the *skull hands* and *feet* reveals that the marrow cavities are widened the cortices are narrowed and there is striking medullary trabeculation especially towards the ends of the diaphyses In the *skull* these changes may give rise to an unusual picture in which the outer table becomes so thin as not to be visible In the greatly widened marrow cavity the bony spicules are arranged as radiating parallel stripes The appearance is that of hair standing on end Changes of this nature in the frontal and malar bones are largely responsible for the mongoloid facial appearance

Diagnosis —See Table 72 (p 1060)

Course —The clinical course is usually steadily progressive Crises similar to those observed in sickle cell anemia or in chronic familial hemo

lytic jaundice are quite unusual unless an infection is present Children who show marked symptoms during the first year of life rarely live to two years of age Others may drag along in a state of chronic ill health for several years before death ensues but few patients live beyond the tenth year Death is often due to an intercurrent infection Whether mild forms of this disease progress to target oval cell syndrome is debatable

Treatment —There is no effective therapy for this condition Splenectomy and hematinics are of no avail Blood transfusions however may prolong life for a short period

VON JAKSCH S ANEMIA

The term von Jaksch s anemia has been dropped from hematologic terminology It was originally described as a relatively benign condition with severe anemia marked leukocytosis the presence of immature and nucleated cells in the peripheral blood and hepatosplenomegaly This blood picture is not characteristic of any one condition It may be noted in Cooley s anemia leukemia chronic infections with a low grade hemolytic element syphilis or iron deficiency

ACUTE HEMOLYTIC ANEMIA OF CHILDHOOD (LEDERER)

An acute hemolytic anemia of unknown origin occurs in children and is known as the acute hemolytic anemia of Lederer

Clinical Manifestations —The onset is sudden with a chill high fever pains in the back and abdomen vomiting prostration stupor rapidly developing anemia and jaundice The urine contains free hemoglobin

Within a relatively few hours there may be a marked fall in the red blood count to 1 000 000 cells The color index approximates unity Spherocytosis and increased fragility of the red cells may occur during the acute phase A marked leukocytosis a shift to the left and the appearance of immature white cells and red cells are noted the liver and spleen may be palpable

Diagnosis —See Table 72 (p 1060)

Treatment —The therapy of this condition consists in the use of blood transfusions Some patients require one transfusion while others may not be helped until several have been given The response may be dramatic and if the patient can be kept alive by transfusion until the hemolytic process is over recovery will occur The return of the blood picture to normal is rapid If three or four transfusions do not stem the tide splenectomy should be performed

ACUTE HEMOGLOBINEMIAS AND HEMOGLOBINURIAS

Acute hemoglobinemias give the manifestations of a hemolytic anemia The types most frequently experienced include

- Hemoglobinuria due to transfusion of incompatible blood
- Paroxysmal hemoglobinuria due to exposure to cold
- Nocturnal paroxysmal hemoglobinuria (Marchiafava Micheli syndrome)
- March hemoglobinuria
- Myoglobinuria
- Blackwater fever
- Acute epidemic hemoglobinuria (Winckel s disease)

HEMOGLOBINURIA DUE TO THE TRANSFUSION OF INCOMPATIBLE BLOOD

The transfusion of blood requires preliminary blood grouping and a cross matching of specimens obtained from donor and recipient (p 3711) Should incompatible blood be transfused due to technical error serious and sometimes fatal reactions occur This mishap may also follow the use of compatible blood in conditions such as familial hemolytic icterus (p 1061) and in pregnancy when unusual hematologic conditions exist

The Hemolytic Transfusion Reaction —The hemolytic transfusion reaction occurs after 50 to several hundred cubic centimeters of incompatible blood have been administered The patient exhibits a sudden shaking chill a rise in temperature to 104° F or more nausea vomiting severe lumbar pain weakness collapse and the appearance of the syndrome of shock

The blood plasma shows the obvious *hemoglobinemia* and the urine is smoky Severe reactions are accompanied by *oliguria* or *anuria* with

TABLE 73 —DIFFERENTIAL DIAGNOSIS OF HEMOGLOBINEMIAS

Variety	Pathognomonic Features
Post transfusion	History incompatible blood with compatible blood in familial icterus and pregnancies with Rh factors (p 1067)
Paroxysmal (p 1075)	Due to cold in syphilitics Donath Landsteiner reaction positive also Rosenbach s test (p 1075)
Nocturnal (p 1075)	*Usually at night Ham test (p 1075) positive hemosiderinuria*
March (p 1076)	Long marches lordosis
Myoglobinuria (p 1076)	Crushing injuries and severe muscle strain
Epidemic Type (p 1076)	In infancy in institutions
Blackwater Fever (p 1076)	In malaria (p 507) treated with quinine (p 517)

gradually increasing *azotemia* *Jaundice* appears the output of urobilin rises and an anemia of varying degree develops with evidences of blood regeneration The patient usually survives the disturbance Death may occur within a few hours from shock or within two weeks from uremia if the renal shutdown cannot be corrected

Foreign protein transfusion reactions are unaccompanied by the blood and urinary changes although the clinical picture may be identical Jaundice does not occur

Treatment —Treatment is directed at the relief of shock by a *continuous intravenous infusion* of saline 5 per cent dextrose or plasma As soon as possible the patient is *alkalinized* to prevent the precipitation of acid hematin in the tubules of the kidney Repetition of the blood transfusion is postponed until expert opinion can be obtained from an experienced hematologist

PAROXYSMAL HEMOGLOBINURIA DUE TO COLD

The most common form of paroxysmal hemoglobinuria is that which results from exposure to cold The precipitating factor in most patients is a chilling of the body or the ingestion of a glass of iced water Almost all these patients have a basic *syphilis* of congenital or acquired origin The blood plasma of luetics contains cold warm hemolysin whereas that of nonsyphilitics contains cold hemagglutinins

Apparently it requires more than the presence of cold hemolysin to cause the disturbance In many syphilitics in whom cold hemolysin is demonstrable clinical symptoms fail to develop even when they are exposed to low temperatures It is thought that the additional factor of vasomotor instability is required

Clinical Manifestations —Paroxysmal hemoglobinuria is characterized by the occurrence of intravascular hemolysis of the red cells with resultant *hemoglobinemia* and *hemoglobinuria* The clinical condition is heralded by recurrent attacks of chilling pains in the abdomen back and extremities vomiting and the passage of a urine of *port wine color* Varying degrees of anemia and acholuric jaundice result from the hematologic disturbance Additionally patients show evidences of a marked vasomotor disturbance such as *urticaria Raynaud s syndrome* or *peripheral gangrene*

Patients exhibiting the urinary phenomenon of blackwater should be referred to an expert for investigation The *Donath Landsteiner reaction* will provide proof of the presence of cold warm hemolysin in the blood serum In the test tube the antibody combines with red cells in the cold and produces hemolysis when the temperature is increased to 37° C Hemolysis also may be produced by immersion of an extremity in cold water (*Rosenbach s test*)

Treatment —Treatment consists of specific therapy for syphilis and transfusions of blood for the restoration of blood volume During the acute attack the urine is alkalinized and fluids are forced to prevent the precipitation of acid hematin in the tubules of the kidney Following treatment for syphilis the autohemolysins persist although paroxysms do not occur even upon exposure to cold

NOCTURNAL PAROXYSMAL HEMOGLOBINURIA (MARCHIAFAVA MICHELI SYNDROME)

The Marchiafava Micheli syndrome of nocturnal attacks of hemoglobinuria occurs in patients who exhibit *chronic hemosiderinuria met hemoglobinemia methemalbuminemia* and excessive increases in the *free hemoglobin* of blood plasma and urine The pathogenesis of this rare condition is stated to be an unusual susceptibility of the red cells to increase in blood hydrogen ion concentration Normally there is a slight acidity in the blood at night due to decrease in pulmonary ventilation This small blood change presumably is sufficient to cause undue nocturnal hemolysis of the red cells

Clinical Manifestations —*Hemoglobinuria* usually occurs only at night but may be observed during the day in lesser amounts It is accompanied by *hemosiderinuria* and *albuminuria* Whereas the hemoglobinuria and the albuminuria are apt to be variable the hemosiderinuria is more constant

Other findings include a severe persistent normochromic anemia leukopenia thrombocytopenia reticulocytosis elevation of *the icterus index* and periods of jaundice The spleen is often palpable

The characteristic laboratory feature of this condition is a marked increase in the fragility of the red cells when exposed to slightly acidified serum (*Ham test*)

Treatment—Treatment consists of transfusions of blood The administration of acidifying salts such as ammonium chloride aggravates the condition It is not advisable to give alkalies and splenectomy has proved valueless

MARCH HEMOGLOBINURIA

Long strenuous marches by young men who are suffering from lordosis may result in the presence of small amounts of free hemoglobin in the urine This may be accompanied by albuminuria and a slight persistent *bilirubinemia*

The condition is innocuous and requires treatment relative to the orthopedic condition

MYOGLOBINURIA

Myoglobinuria results from a variety of dissimilar conditions It occurs after *crushing injuries* to the body it has followed the ingestion of fish that had been toxified by cellulose resinous acids (Haff disease) It may appear in severe muscular disorders of humans and in draught horses who have been worked strenuously after a period of rest

The excretion of myohemoglobin in the urine denotes disintegration of skeletal muscle and may be associated with profound paralysis The myohemoglobin is identified by spectroscopic examination *Therapy* consists of forcing fluids and alkalinization of the urine to prevent the deposition *of crystals in the tubules of the kidneys*

BLACKWATER FEVER

Blackwater fever occurs in the course of malignant estivo autumnal *malaria* It may be due to sensitization to the parasite or to some abnormal response to the administration of quinine *The disturbance is most* commonly observed in persons who have lived in malarial regions for only a relatively short period It may occur before or after the administration of quinine In severe examples the mortality is high and patients are not to be given quinine again

See *Malaria Treatment of* (p 522)

ACUTE EPIDEMIC HEMOGLOBINURIA (WINCKEL S DISEASE)

Acute epidemic hemoglobinuria is a rare and fulminating disorder that *has been observed in* institutionalized newborn infants It is characterized by jaundice cyanosis fever and smoky urine which contains free hemoglobin Postmortem examination reveals extensive punctate hemorrhages in most of the internal organs The cause is unknown although there is some evidence that the syndrome results from sepsis The prognosis is poor but the infant may be sustained *by small transfusions*

ANEMIAS DUE TO DISTURBANCES OF THE MATURATION FACTOR

The *intrinsic* and *extrinsic factors* required for the normal maturation of the red blood cells have been described (p 1038) The intrinsic factor

is secreted by the stomach and duodenum the extrinsic factor is supplied in the diet Absorption of both factors occurs in the upper bowel and storage takes place in the liver and kidneys Any dislocation of this complicated economy results in the clinical manifestations of a *hyperchromic macrocytic anemia* Premature and imperfect non nucleated red cells are seen in the peripheral blood megaloblasts rarely appear when the condition is further advanced

Quite obviously hyperchromic anemia may arise through the operation of various agencies In *idiopathic pernicious* or *Addisonian* anemia the fundamental disturbance is diminution or absence of intrinsic factor Other hyperchromic anemias result from diminution or absence of extrinsic factor in the diet Interference with absorption of both principles may be due to inflammatory diseases of the intestines and storage abnormalities in severe damage to the liver and kidneys

MACROCYTIC HYPERCHROMIC ANEMIA (ADDISON S BIERMER S PRIMARY OR PERNICIOUS ANEMIA)

Macrocytic hyperchromic anemia is the most common example of a clinical entity resulting from a deficiency of hematopoietic principle The disturbance is a chronic disease of middle and advanced years affecting females and males equally Except for certain neurologic symptoms practically all manifestations disappear after the continued administration of *liver extract* Cessation of therapy for a prolonged period results in a severe or fatal reaction

Clinical Manifestations —Pernicious anemia often remains asymptomatic for many years Despite a markedly diminished red cell count the patient maintains surprisingly good health due to adjustment of the organism to the insidious changes Later hematologic gastro intestinal and neurologic symptoms develop The onset is always vague with a protracted history of progressive weakness dyspepsia gastro-intestinal symptoms pallor a subicteric or definitely icteric component headache dizziness inability to concentrate visual disturbances tachycardia dyspnea or edema

Gastro intestinal Symptoms —The gastro-intestinal manifestations are characterized by atrophic changes in the digestive tract Often the herald symptom is an irritation of the tongue buccal mucous membrane pharynx or esophagus The highly suggestive *hunterian glossitis* manifests itself by redness vesiculation ulceration and fissuring Often without objective manifestations the patient complains of persistent *glossodynia* (p 1687) especially after taking hot or spicy food In the latter stages the typical *atrophic glossitis* (p 1676) becomes manifest the tongue is pale flabby is shiny and polished and the papillae are no longer recognizable These changes are most marked on the anterior half of the organ and along the edges The sense of taste is usually impaired although the atrophic tongue may occur asymptomatically

Changes of a nature similar to the glossitis occur also in the stomach eventually the patient presents an *atrophic gastritis* (p 1810) that is most marked in the fundic region The symptoms referable to the gastritis are often surprisingly vague considering the extent of the pathologic lesion There may be no disturbance whatsoever or at most there are complaints

of epigastric fulness bloating heartburn' gaseous eructations anorexia nausea occasional vomiting flatulence diarrhea or constipation Gastric analysis reveals complete *histamine anacidity* The volume of gastric juice is greatly diminished Intrinsic factor and gastric enzymes are absent or present only in traces Following adequate therapy very minor changes occur the volume of gastric juice may be somewhat increased but no improvements in the acidity and enzymatic activity are demonstrable

Neurologic and Psychiatric Manifestations—The neurologic and psychiatric aspects of pernicious anemia are varied All divisions of the nervous system brain spinal cord or peripheral nerves may be involved A frequent presenting symptom is symmetrical *numbness* and *tingling of the extremities* due to peripheral neuropathy This symptom may occur without objective neurologic findings and the early stages of it are reversible under adequate therapy

Combined degeneration or subacute combined *degeneration of the spinal cord* is often first suggested by absence of the vibratory sense which is soon followed by disturbances in the protopathic characteristics of joint and muscle sensibility These often cause the patient to note the sensation of walking on velvet When vision is not keen the disturbed muscle sense produces unsteadiness or falling when the eyes are closed as in washing the face or walking in the dark

Involvement of the *posterior and lateral columns* of the spinal cord usually produces spasticity ataxia weakness hyperreflexia a Babinski sign and absent superficial reflexes in the abdominal and cremasteric regions The fully developed clinical picture is that of a *spastic ataxia* with the legs more severely involved than the arms

If the involvement is more marked in the region of the posterior column areflexia and *flaccidity* may supervene *Loss of sphincteric control* is not common but may occur in severe instances Under these conditions there is marked constipation distention of the urinary bladder and overflow incontinence The sensory disturbances may take the form of a glove and stocking hypalgesia and hypesthesia Girdle sensations and diffuse pains are uncommon but episodes analogous to the crises of tabes (p 1464) are observed Cranial nerve involvement is decidedly unusual

Psychiatric changes occur with fair frequency and paranoid psychoses may develop It is not clear whether an etiologic relationship exists between the anemias and the mental changes

In most instances the neurologic manifestations are detected later than the gastro intestinal or hematologic components However the nervous manifestations occasionally constitute initial symptoms whose nature is not clarified until the gastric analyses and blood findings have been obtained

Blood Findings—The hemogram furnishes incontrovertible evidence of the presence of a primary anemia It is the best guide to the progress of the disease and the response to therapy

The *erythrocyte count* is diminished disproportionately to the clinical symptoms It may be as low as 1,500 000 in patients who have few complaints and counts below 1 000 000 are not unusual Together with the reduction *in the numbers* of the red blood cells the *hemoglobin percentage* falls but not in proportion so that the *color index* is invariably greater

than unity and may approach 2 *Leukocytes* and *thrombocytes* are pro portionately decreased the former to the region of 2500 per cu mm and the latter to 100 000 or less The white cells show a relative lymphocytosis and a shift to the right A marked *eosinophilia* is observed when large amounts of raw liver are given orally Hypersegmented polymorpho-nuclear leukocytes are usually observed in the stained spreads (macro polycyte)

The stained blood smear discloses the most marked abnormalities *Anisocytosis* is observed but the most characteristic change is the *increase in red cell diameter* Erythrocytes are *macrocytic* oval in shape and well filled with hemoglobin so that there is often not even a small area of cen tral pallor The variations in size and shape are accompanied by staining

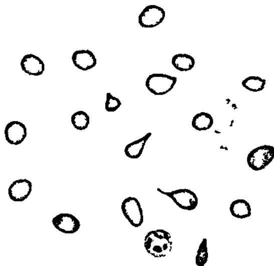


Fig 232—Pernicious anemia during relapse (Wright s stain)

abnormalities *polychromatophilia stippling* and *reticulation* are seen in perhaps 2 per cent of the cells Nuclear remnants such as the Cabot rings and Howell-Jolly bodies are observed at times and an occasional normo blast or megaloblast is found In the era before the advent of liver ther apy blast crises were observed with large numbers of nucleated cells in the peripheral blood See Figs 227 230

The marrow spread is characterized by a marked increase in megalo blasts and abnormalities in the segmentation and size of the metamyelo cytes During a relapse there is elevation of the icterus index the van den Bergh reaction is indirect urinary and fecal urobilinogen excretions are increased and the blood cholesterol is low The basal metabolic rate is

normal or diminished With a severe anemia evidences of a *prerenal azotemia are encountered*

Other Physical Findings—Besides the characteristic changes in the gastro intestinal nervous and hematologic structures the examination of the patient with pernicious anemia reveals other findings *Pallor icterus* and *hemic murmurs* are noted The patient shows remarkably little change in general nutrition and there is very little weight loss The liver is not often enlarged the spleen is rarely palpable and lymphadenopathy is not present

With manifestations of severe anemia abnormalities in the *electrocardiogram* are observed These include tachycardia low voltage and inversion of the T waves At this time there may be symptoms of backward *cardiac failure* such as dyspnea mild pulmonary edema congestion of the liver and edema of the extremities Tenderness of the sternum may be present and brownish pigmentation and purpura occur at times

As is common with other severe anemias the relapses in pernicious anemia are invariably accompanied by an irregular pyrexia (anemic fever) Temperatures may range as high as 102° F but rarely a sub normal temperature is observed

The patient with pernicious anemia quite regularly presents certain characteristic constitutional aspects The hair tends to gray prematurely the eyes are widely set apart and the subcostal angle is widened That this habitus is on an hereditary and familial basis is further attested by the incidence in blood relatives of anemia and anacidity

Diagnosis—The differentiation of macrocytic from other varieties of anemia is shown in Table 71 (p 1058)

The manifestations of macrocytic hyperchromic anemia simulate those of many neurologic gastro intestinal and malignant diseases The safest method of avoiding serious errors is to maintain a high index of suspicion regarding pernicious anemia and perform *complete blood studies* in all chronic obscure diseases that involve manifestations in the digestive or nervous systems Should there still remain a reasonable doubt as to the presence of a primary blood disorder the results of the *therapeutic test with liver extract* (p 1081) are most convincing

Course—The uncomplicated course of pernicious anemia which culminated fatally is no longer observed since the introduction of *liver extract* Previous to this time the disturbance was characterized by remissions and exacerbations of unknown causation Eventually however despite the liberal use of transfusions the patient succumbed usually within ten years of the onset of symptoms The introduction of liver extract therapy has modified completely this ominous outlook With continued and adequate therapy life expectation and usefulness need not be modified provided that treatment is initiated before severe neurologic complications have occurred

Associated Conditions—Macrocytic hyperchromic anemia is often associated with other common diseases of middle life Diabetes mellitus cholelithiasis arteriosclerosis and gastric malignancy seem to occur with increased frequency

Diabetes Mellitus—Severe and uncontrolled diabetes may upset the management of the patient with pernicious anemia The requirement for

liver extract is increased with glycosuria and the carbohydrate tolerance of the diabetic suffers with the onset of the hematologic condition There is fortunately no antagonism between liver extract and insulin

Arteriosclerosis —The symptoms of cardiac failure which results from a profound anemia are enhanced by the simultaneous presence of an arterio sclerosis The vascular disease may increase the requirements for liver extract

Cholelithiasis —As in all other conditions accompanied by excessive destruction of blood there is an increased tendency toward the develop ment of gallstones This fact however in no way alters the diagnostic picture or the therapeutic program

Carcinoma of the Stomach —Carcinoma of the stomach is certainly more common in patients with pernicious anemia than in the general population This is probably related to the atrophic gastritis that accom panies the blood disturbance The discrepancy may be partially due to the factor of error since an insidious gastric malignancy may masquerade as a primary anemia for a considerable period of time (p 1814)

The presence of the malignancy is suspected if the patient loses weight and has persistent blood in the stool and in the gastric specimen The *radio graphic investigation* usually delineates the defect under which circum stance surgical therapy is initiated after the blood has been restored to normal by adequate liver therapy and transfusions The insidious devel opment of a hypochromic anemia in a patient with pernicious anemia treated with liver extract usually means that a carcinoma of the stom ach is superimposed

Treatment —The treatment of pernicious anemia with the *hematopoi etic principle* is so pecific as to constitute a *therapeutic test* The admin istration of a potent substance brings about symptomatic improvement within forty eight hours and if adequate dosage is continued indefinitely maintains the recovery

As soon as the diagnosis of pernicious anemia has been established 10 to 15 injectible units of liver extract (U S P) are given intramuscularly into the buttocks This is repeated twice for two weeks and then once weekly for eight to ten weeks At the end of this time barring complica tions the peripheral blood count returns to normal and a maintenance daily dose of 1 injectible unit is continued For purposes of convenience the maintenance do e may be administered at weekly or fortnightly in tervals in the first instance 7 units and in the latter 14 units are given at each injection Thi is continued for the remainder of the patient s life Those patients who object to injection therapy can be given oral prepa rations it requires 250 to 500 gm of crude liver to supply the anti anemic potency of 1 injectible unit

Criteria of Satisfactory Therapy —With adequate therapy there is considerable improvement within forty eight hours Shortly thereafter the *reticulocyte count* rises and reaches its height by the eventh to tenth day following the initiation of treatment In general the success of therapy is measured by the total number of circulating reticulocytes which should number between 250 000 and 400 000 per cu mm at the crest of the re action If the initial red blood count i over 3 000 000 the reticulocyte in crease is irregular

After from eight to ten weeks of therapy the red count should reach at least 4 500 000 The size and shape of the red cells return to normal and the symptoms of the active anemic state disappear although the *anacidity and certain of the neurologic manifestations persist*

If a definite case of pernicious anemia fails to react favorably or completely to liver extract the fault may lie in a hypothyroid state The additional administration of *thyroid extract* (p 1189) may then effect complete recovery

Manifestations of Inadequate Therapy—With a failure of response to treatment the practitioner first suspects the accuracy of his diagnosis and then the potency of the preparation When he has satisfied himself on both of these scores he searches for some complicating factor such as diabetes, an infection or a neoplasm

Complications of Therapy—Occasionally the sensitized patient develops *allergic responses* to liver extract These are manifested by the appearance of eosinophilia severe pruritus urticaria asthma and anaphylaxis Under such circumstances the practitioner uses another brand of liver extract preferably one prepared from a different animal since hog cattle and horse preparations are commercially available If this maneuver proves unsuccessful *desensitization* (p 563) becomes necessary, employing small doses at frequent intervals With persistence of the untoward manifestations the oral preparations of *whole liver or stomach are substituted*

A more serious but fortunately rare complication of liver therapy is the occurrence of a *toxic hepatitis* which may run a prolonged course with eventual recovery Peculiarly enough liver extract may be reexhibited to these patients without a recurrence of the hepatitis

Gastric Preparations (*Ventriculin*) —The dried defatted stomachs of *the hog or the pyloric ends of the stomachs of cattle or sheep* have been prepared in powdered form An average daily dose of these is 10 to 40 gm in order to induce and maintain remission in pernicious anemia The material is bulky and unpalatable absorption is poor and this form of oral therapy does not compare in efficiency and economy with the use of injectible extract

Liver and Oral Liver Extracts—Besides the injectible liver preparations whole liver uncooked or partially cooked induces and maintains a remission if given orally in the dosage of approximately one pound daily Powdered liver extract *is also available and 7 to 25 gm are the equivalent* of one injectible unit Oral therapy is irregular and expensive and is not comparable to the efficiency of injectible extract

Hydrochloric Acid—Most patients do not require gastric acid but it is wise to suggest the administration of at least 4 cc (1 dram) of *Dilute Hydrochloric Acid* before and with each meal The preparation is mixed with a wineglass full of sugared water and taken through a glass tube in order to protect the teeth *Glutamic Acid Hydrochloride* available in 1 gm capsules is a more elegant and more expensive form of substitution therapy

Transfusion of Blood—Before the introduction of liver extract, blood transfusion therapy was adequately tested and resulted in the relief of some symptoms but no significant alteration in the course of the disease At present it is apparent that transfusions are of mere accessory impor

tance Their use is reserved for patients with complications or those who present themselves with a profound anemia that requires immediate correction Transfusion does not substitute for liver extract therapy the two forms of therapy may be given simultaneously

Iron—The administration of iron in pernicious anemia is futile unless there is a superimposed iron deficiency Under these circumstances in addition to the liver extract *Ferrous Sulfate* is administered in a daily dose of 1–2 gm (15–30 grains)

Diet—The patient with pernicious anemia requires only a normal balanced diet (p 658) If there are evidences of vitamin deficiency particularly of nicotinic acid and riboflavin synthetic vitamin preparations are administered With profound neurologic manifestations 100 mg (1½ grains) of *thiamine chloride* are administered intravenously each day in the hope of effecting symptomatic relief

Folic Acid—Synthetic folic acid a fraction of vitamin B complex may prove to be the missing *extrinsic factor* in hyperchromic anemia Administrations of 5 to 20 mg daily produce reticulo-cytosis in the manner of liver extract The therapeutic implications of these effects may prove important

SYMPTOMATIC HYPERCHROMIC ANEMIA

Symptomatic forms of hyperchromic anemia are associated with organic lesions of the digestive tract pregnancy diffuse liver and kidney diseases hypothyroidism tropical macrocytic anemia tropical and nontropical sprue and blood dyscrasias

Organic Diseases of the Digestive Tract—Hyperchromic anemia accompanies extensive disease or operative removal of the stomach Following *subtotal or total gastrectomy* a hypochromic anemia occurs within a few months Two or three years later a hyperchromic anemia may develop due to loss of the glandular secreting surface that produces intrinsic factors

Macrocytic anemia also may be associated with digestive diseases that interfere with absorption of intrinsic and extrinsic factors In *regional ileitis chronic colitis pellagra* and *fistulas* through which intestinal secretion is lost intrinsic and extrinsic factors are prevented from reaching the circulating blood stream

The status of the anemias that occur with *Diphyllobothrium latum* infestations (p 1893) is not clear In some patients expulsion of the worm is sufficient to correct the blood condition others however require the administration of liver extract or folic acid

Pregnancy—Most anemias of pregnancy are hypochromic (p 2646) In certain women however a typical macrocytic anemia develops in mid pregnancy The *pernicious anemia of pregnancy* differs from the true idiopathic variety in that there may be acid in the gastric contents tongue signs are meager and provided that the blood picture has returned to normal therapy can be discontinued after delivery

Liver extract is administered as in primary hyperchromic anemia or folic acid is substituted Transfusions are required only if the red cell count falls below 1 000 000 per cu mm

Tropical Macrocytic Anemia—Tropical macrocytic anemia resembles the

pernicious anemia of pregnancy It is mostly dependent upon a reduction of the amount of extrinsic factor in the diet The condition has been de scribed in pregnant Indians who subsist on a deficiency diet The disturb ance responds to the administration of autolyzed yeast concentrates crude liver extract or folic acid

Tropical and Nontropical Sprue—Sprue is a disease of importance in the tropics and is occasionally seen in temperate climates It is conventionally divided into tropical and nontropical varieties the latter being synony mous with *celiac disease* (Gee s Disease) or *idiopathic steatorrhea* (p 1938)

Tropical sprue occurs particularly in visitors from cooler climates who find native food unpalatable and subsist on canned foods sweets and cereals *Nontropical sprue* is seen in children and occasionally in adults

Clinical Manifestations—Sprue occurs at a younger age than pernicious anemia The symptoms are those of pernicious anemia but the principal manifestations are the severe *gastro intestinal symptoms* The patient passes pale foul greasy stools *these contain large amounts of split and* unsplit fat calcium soaps and fat soluble vitamins There are progressive loss of weight and strength flatulence abdominal distention and evidences of deficiencies of calcium and vitamins A D and K Stomatitis glossitis proctitis and vaginitis are common and severe Cachectic edema occurs in long standing cases Tetany osteomalacia hyperkeratinization of epithe lial structures skin changes and hemorrhages may occur

Radiography—Radiographic study often reveals abnormalities of small intestinal motility and bizarre mucosal patterns with localized dilatation and puddling of the contrast medium *These changes are by no means* specific although they usually do not occur in pernicious anemia Whether they are the cause of sprue or are an expression of the multiple deficiencies which arise in this disease is not clear

Laboratory Data—Gastric analysis usually reveals the presence of free hydrochloric acid The hemogram is variable The blood may be nor mal but there is often a hypochromic anemia and relatively infrequentl a macrocytic hyperchromic anemia The latter is indistinguishable from Addisonian pernicious anemia but usually is of less severity and the macro cytosis is not marked The bone marrow may be megaloblastic evidences of excessive hemolysis present in Addisonian pernicious anemia are not present as a rule in sprue The blood calcium is reduced and as a result of malnutrition the blood proteins are low

The *dextrose tolerance test* (p 3716) aids in differentiating sprue from pernicious anemia In pernicious anemia a fairly normal dextrose toler ance test is obtained in sprue there is flat sugar curve since the rise in blood sugar that normally follows the ingestion of dextrose does not occur That this is due to malabsorption is apparent from the normal curve after intravenous injection of the sugar

Course—The course of sprue is variable In young children recovery follows proper dietotherapy and protection from infection In adults the disease lasts for years and is subject to exacerbations and remissions for unknown reasons

Treatment—The patient with macrocytic anemia may respond well to parenteral injections of crude liver extract or of folic acid (p 1083) Special diets (p 674) high in protein and low in glucose and fat are recom

mended The banana diet is particularly useful The liberal parenteral administration of vitamins is advisable If the response to therapy is poor a chronic *fibrosis of the pancreas* (p 2785) is suspected and the enzymatic content of the duodenal contents is estimated In sprue this test reveals normal findings whereas in chronic pancreatic disease enzymes may be absent Similar clinical pictures may be seen rarely in tabes mesenterica the lymphoblastomas and chronic inflammatory diseases of the small intestines or mesenteric lymph nodes

Advanced Parenchymal Disease of the Liver and Kidneys —With advanced *hepatic cirrhosis* (p 1969) and in the late stages of *chronic nephropathies* (p 2362) hyperchromic anemias may be observed due to inadequate storage of hematopoietic principle or excessive hemolysis Treatment with liver extract holds little promise since the fundamental disturbances are of such severity that no form of therapy can be expected to be attended with success

Myxedema —Almost half of the patients with myxedema exhibit marked interference with gastric secretion When this disturbance is combined with a deficient food intake macrocytic hypochromic or microcytic anemias may develop The anemia is usually not severe and responds to iron liver and thyroid extract

One mild type of macrocytic anemia in myxedema is corrected solely by administration of thyroid extract The macrocytosis in these cases is moderate and uniform lacking the anisocytosis and poikilocytosis of true pernicious anemia

Achrestic Anemia —Achrestic anemia is ascribed to a lack of utilization of the liver extract principle It is characterized by a severe macrocytic hyperchromic blood picture a megaloblastic bone marrow slight leukopenia thrombocytopenia a progressively downhill course and lack of adequate response to liver extract therapy Free hydrochloric acid may be present in the gastric juice

Blood Dyscrasias —In congenital and acquired hemolytic anemias (p 1060) a pseudomacrocytosis and pseudohyperchromia may be caused by the intense reticulocytosis that occurs when hemolysis is active Reticulocytes are larger than adult erythrocytes and account for the spurious macrocytosis

Macrocytosis is also observed in aregenerative or refractory anemia (p 1090) myelophthisic anemia (p 1091) erythroblastic anemia (p 1071) and erythroblastosis foetalis (p 1067)

IRON DEFICIENCY ANEMIAS

There is a constant flux in iron metabolism (p 606) as a result of the continuous destruction of red blood cells and their replacement by young erythrocytes In these processes hemoglobin is broken down and resynthesized In the bone marrow iron is combined with pyrrole complexes and protein to form hemoglobin so that there is practically no excretion of endogenous iron The result of this efficient arrangement is the small daily iron requirement of 15 mg for adult women or growing children and 5 mg for the adult male The additional amounts required by the female are due to the demands of pregnancy menstruation and lac

tation Children need extra amounts during the growth periods of infancy and puberty

Anemias due to lack of iron can *conceivably arise from inadequate iron* intake poor iron absorption increased loss of iron from the body and interference with the utilization of iron In practice it requires the combination of an inadequate iron intake and an increased demand to effect a significant iron deficiency the common examples of which include the physiological anemia of the newborn the nutritional anemia of infancy chlorosis of adolescent females anemia of pregnancy anemia due to chronic blood loss and the idiopathic hypochromic anemia of older women Iron deficiency anemias in the adult male except for those due to chronic blood loss are of great rarity attesting to the efficiency of the utilization of iron under normal circumstances

Abnormalities in digestion and absorption are of relatively slight importance in the metabolism of iron The most important factor is the hydrochloric acid of the gastric contents although it is amazing to note the infrequent occurrence of anemia with complete anacidity or subacidity Intestinal disturbances are occasionally related to iron deficiency Anemias are common in intestinal infestation particularly with the tapeworm hookworm and Diphyllobothrium They also occur with deficient absorption as in sprue chronic enteritis enterocolitis and intestinal fistulas

The Response of Bone Marrow —The initial response of the bone marrow to iron deficiency is the output of normally sized erythrocytes containing a reduced amount of hemoglobin As the anemia continues *microcytosis* occurs and still later, less and less pigment is allotted to each cell until there is only a thin rim to be distinguished The marrow functions excessively as reflected by the *normoblastosis* (Fig 227)

The peripheral blood count reveals these changes by a diminution in the hemoglobin percentage and a fall of the color index to below unity Later when the marrow puts out smaller cells there is a *hypochromic microcytic anemia* with a slight reduction in the numbers of the white blood cells and platelets The differentiation of iron deficiency anemia from other varieties is shown in Table 71 (p 1058)

THE PHYSIOLOGICAL ANEMIAS OF INFANCY

The infant develops a physiological anemia due to mechanical and hematopoietic factors The normal red count of the newborn averages 5 000 000 cells per cu mm If the cord is tied off immediately after birth a large volume of blood remains in the placenta and the infant suffers an anemia from mechanical cause in the manner of a hemorrhage

A later type of physiological anemia is marked by a progressive fall of the red count for the first two or three months of life A level is reached at about 4 500 000 cells with 60 to 75 per cent hemoglobin and this remains constant for the first two years after which there is a progressive rise to adult figures This gentle but protracted anemia results from the shift of the hematopoietic functions from extramedullary centers to bone marrow It is a normal abnormality It is not influenced by hematinics and indeed requires no treatment

The differential diagnosis of infantile anemias appears in Table 74 (p 1087)

NUTRITIONAL ANEMIA OF INFANCY

In the second half of the first year there may appear an anemia de pendent upon iron deficiency This is most commonly observed in the premature infant in twins or in children born of mothers who exhibited a hypochromic anemia during the period of gestation

In each of these states the hemoglobin level is normal at birth but as the stores of iron which accumulated in the fetus during the intra uterine life are depleted the anemia develops particularly if the child is given a diet consisting entirely of milk The predisposition of certain in

TABLE 74—ANEMIAS OF INFANCY AND CHILDHOOD

Variety	Pathognomonic Findings
Physiological (p 1086)	In newborn Hypochromic type
Physiological (p 1086)	After 2 to 3 months Hypochromic type
Nutritional (p 1087)	After 6 months Hypochromic type in milk fed
Erythroblastosis Foetalis (p 1067)	Hemolyt in newborn Intense jaundice erythroblasts in stained spread Rh factors in maternal and paternal bloods (p 1067)
Sickle Cell (p 1065)	In Negroes Changes in unstained blood (sickling) target cells jaundice splenomegaly leg ulcers
Cooley s Anemia (p 1071)	In Mediterranean children Target cells jaundice splenomegaly
Lederer s Anemia (p 1073)	Hemolytic n children Jaundice rapidly progressing anemia
Epidemic Hemoglobinuria (p 10 6)	In newborn With sepsis urine discoloration jaundice
Congenital Anemia (p 106)	In newborn Large liver and spleen but no jaundice Rh factors (p 1067)
Hemorrhagic Disease of Newborn (p 1111)	Bleeding specific response to menadione (p 630)
Hemophilia (p 1118)	In males Family history increased coagulation tim

fants to develop anemia depends in large measure on the size of the fetal iron reserves

Clinical Manifestations —The child may not evidence any manifestations of the anemia unless repeated infection calls the condition to the attention of the mother or the practitioner Under these circumstances it is often dif ficult to decide whether the anemia lowered resistance so that infection was invited or whether the sequence involved a primary infection with a second ary anemia In either event the children become pale they fail to gain weight and lack normal vigor They fret and whine the appetite is poor and digestive disturbances are common Development may be retarded

Examination reveals no abnormality beyond a palpable spleen The red count may be as low as 2,500 000 cells with hemoglobin values at 25 per cent White cells and platelets are usually depressed The stained spread

discloses the increased central pallor of the erythrocytes with anisocytosis and poikilocytosis

Treatment—Treatment requires the oral administration of *Ferrous Sulfate* in 100 mg doses (1½ grains), given three times daily *Saccharated Ferrous Carbonate* may be mixed with food in a dose of 0 32–0 65 gm (5 to 10 grains) three times daily Additionally, the child s diet is supplemented with mashed liver, prunes or apricots which are high in iron content (p 607) The use *of liver extract and other hematinics is not* advisable

Susceptible children such as prematures twins and infants born of anemic mothers should receive iron prophylactically during the third or fourth months of life The diversification of the diet is also inaugurated at an earlier date

GOAT S MILK ANEMIA

In continental countries a macrocytic anemia has been described in infants who are fed goat's milk The exact cause of the anemia is not known but it is often associated with poor nourishment and a chronic diarrhea The anemia may be cured it is said by administering liver or yeast extract

CHLOROSIS

Chlorosis is the hypochromic anemia of adolescent girls It was formerly a common clinical condition but we have no current records of authentic examples It has been attributed to the combined influences of inadequate diet, rapid growth and blood loss due to menstruation

Clinical Manifestations—Chlorosis was characterized by a peculiar greenish pallor weakness loss of weight a low grade pyrexia restlessness and emotional and vasomotor instability

Physical examination revealed no consistent abnormality The erythrocytes varied between 3 000 000 and 5 000 000 cells with a markedly reduced hemoglobin giving a color index as low as 0 4 The total white count was proportionately decreased and a relative lymphocytosis was often present A stained spread revealed a central pallor of the erythrocytes hyperacidity of the gastric contents was a frequent finding

Treatment—The response of chlorosis to the oral administration of inorganic iron was reported to be dramatic *Ferrous Sulfate* 1 2 gm (18 grains) daily was prescribed until the blood count had returned to normal

THE PHYSIOLOGICAL ANEMIA OF PREGNANCY

In a normal pregnancy plasma volume increases due to an augmentation of the fluid component As a result there occurs a relative reduction in the red blood count to 4 000 000 while the hemoglobin falls to the vicinity of 70 per cent The differentiation from other anemias of pregnancy appears in Table 75 (p 1089)

Physiological anemia produces no symptoms and requires no treatment

THE HYPOCHROMIC ANEMIA OF PREGNANCY

In the second half of pregnancy *hemoglobin levels may fall as low* as 50 per cent or less The anemic state is due to the interplay of several factors there is a temporary reduction or complete absence of gastric acid

ity during pregnancy the growing fetus requires an additional supply of iron from the maternal organism iron rich foods are often lacking in the diet particularly if there has been any considerable toxemia of pregnancy (p 2638)

Clinical Manifestations —The hypochromic anemia of pregnancy causes pallor malaise flatulence capricious appetite easy fatigability and brittleness of the finger nails The peripheral blood count reveals a hemoglobin of 50 to 60 per cent or less with a color index of 0.5 to 0 8 Should the anemia be more profound than this other factors are sought

Treatment —Therapy requires only the administration of *Dilute Hydrochloric Acid* (N I) and *Ferrous Sulfate* in dosages of 1 2 gm (18 grains) daily The diet is increased to include foods of high hemoglobin regenerative power (p 1052) At the termination of pregnancy medication is stopped as soon as the hemogram is normal Reversion to anemia suggests the operation of some other facto

IDIOPATHIC HYPOCHROMIC ANEMIA

Idiopathic hypochromic anemia occurs in middle aged women The origin of the disturbance may depend on several factors anacidity probably

TABLE 75 —THE ANEMIA OF PREGNANCY

Variety	Pathognomonic Findings	Treatment
Physiological (p 1088)	In early months Hypochromic due to increased plasma volume	None
Hypochromic (p 264)	In second half Hemoglobin less than 50% subacidity or anacidity	Acid and iron
Hyperchromic (p 2616)	High color index but no glossitis or anacidity	Liver extract

interferes with the ionization solution and eventual absorption of the iron from the intestinal tract many patients because of their neuroses partake of unbalanced diets and develop vitamin deficiencies blood loss from the menorrhagia that is so common at the menopause accounts for part of the iron deficiency

Clinical Manifestations —The anemia commences insidiously and symptoms are often of considerable duration by the time the physician is consulted The usual complaints include faintnes weakness undue susceptibility to cold or infection paresthesias painful tongue menorrhagia and disturbances in swallowing the last suggesting the Plummer Vinson syndrome (p 1728) Many patients note brittleness of the finger nails In other instances the nails become oft and bend or break Depressions in the center of the dystrophic nails give rise to koilonychia a spoonlike deformity Many women have complaints referable to the gastro intestinal tract they note epigastric distress fullness nausea and constipation

Physical examination usually discloses premature grayness the patient is often highly nervous and pale the tongue has a glazed appearance hemic murmurs are heard there is a gastric anacidity the liver spleen and lymph nodes are not abnormally enlarged Gastroscopy reveals atrophy

of the mucous membrane and spasm or web like formations in the esophagus Except for hypochromia and microcytosis the hemogram is normal

Treatment —Treatment is effectively carried out by the administration of iron and supplementary vitamins particularly B complex Substitution therapy with hydrochloric acid is advisable Excessive menstrual bleeding may be curbed by injections of androgen (p 2401) or by roentgen therapy

ANEMIAS DUE TO INTRINSIC DEFECTS OF BONE MARROW

Anemias due to intrinsic bone marrow defects present an ominous prognosis since all the processes of erythrogenesis and myelopoiesis are disturbed The more hopeful *aplastic anemias* result from idiopathic toxic and infectious causes With the *myelophthisic anemias* due to organic replacement of bone marrow the prognosis is hopeless and little can be done other than to attempt to keep the patient alive by repeated transfusions

APLASTIC ANEMIA (HYPOPLASTIC ANEMIA AREGENERATIVE ANEMIA)

A variety of etiologic agents may produce the symptom complex of aplastic anemia Essentially it consists of a severe normochromic anemia leukopenia a relative lymphocytosis and a thrombocytopenia The bone marrow in the classical form is made up of yellow fatty hypocellular tissue In a few scattered areas small foci of normal hematopoietic tissue are seen All gradations from hypocellular fatty marrow to active appearing hyperplastic bone marrow may be observed

Etiology —Aplastic anemia results from idiopathic toxic or infectious causes

Idiopathic Aplastic Anemia —Idiopathic examples of aplastic anemia are seen in children young adults and older patients In the young it is likely that the marrow is congenitally deficient or it may be destroyed by some unknown toxic agency In the older group in addition to these possible etiologic factors there may be an element of liver extract deficiency

The idiopathic examples of aplastic anemia tend to run a chronic course Often the disturbance is punctuated with severe hemorrhages In the more favorable instances spontaneous remissions are observed but they are usually transitory

Aplastic Anemias Due to Chemical Agencies —Aplastic anemia is produced by chemical agencies *In industry* the syndrome is most frequently caused by benzol derivatives and radium The occupations that are apt to cause anemia from exposure to benzol derivatives include those that deal with rubber canning photography painting leather and printing In these the toxic agent enters the body by inhalation there is considerable variation in the predisposition to the affliction

In medicine this complication follows radiation therapy tridione the administration of arsenicals gold sulfonamides and dinitrophenol The disturbance may also follow exposure to *chemicals* in hair dyes and volatile insecticides

Although the aplastic anemias of chemical origin are apt to run an acute course their prognosis offers some hope of recovery if the toxic cause is recognized and removed

Aplastic Anemia Due to Infection —In long standing chronic or overwhelming acute infections an aplastic anemia may be observed

Clinical Manifestations—The suspicion of the presence of an aplastic anemia arises when the patient presents an extreme pallor and subjective symptoms that include weakness dizziness inability to concentrate giddiness easy fatigability tachycardia and dyspnea on exertion Hemorrhagic tendencies of varying degree are present depending on the extent of the reduction in the platelet count With a severe leukopenia necrotic and gangrenous inflammations are observed in the body orifices

The acute aplastic anemias are characterized by a stormy course with severe hemorrhages purpura and terminal fusospirochetal infections In those of longer duration the progressive and obstinate anemia is the outstanding clinical manifestation

Physical examination reveal no important abnormality there is no enlargement of the liver spleen or lymph nodes

The Hemogram—The blood picture is a variable in aplastic anemia There may be evidences of a severe normochromic or macrocytic anemia Correspondingly the marrow shows gradations from an almost acellular state to one of hyperactivity in which there are large numbers of giant cells An occasional tendency to excessive hemolysis is observed with low grade jaundice and the usual clinical and laboratory evidences of increased blood destruction

In the chemical anemias the first hematological abnormality is not a leukopenia as was formerly believed macrocytosis and evidences of bone marrow stimulation are usually observed in the peripheral blood Disturbances due to arsenicals and gold salts are more often featured by platelet deficiency (p 1114) and resultant bleeding and purpura

Treatment—The treatment of patients with aplastic anemia is initiated by the attempt to discover and eliminate the fundamental etiologic factor Meantime *blood transfusions* are used liberally *hematinics* and *vitamin preparations* are given orally and *liver extract* is injected intramuscularly *Splenectomy* is a futile procedure Exposure to stimulating doses of *x ray* carries some danger and seems inadvisable except as a measure of desperation

The various extracts of *spleen bone marrow* and *fetal liver* have failed to demonstrate their hypothetical advantages *Hyperthermia* may be attempted but thus far the results have not been promising *Normal bone marrow* from a compatible donor may be injected into the sternal marrow cavity This form of therapy has theoretical advantages but the results thus far are not striking

MYELOPHTHISIC ANEMIA (LEUKO ERYTHROBLASTIC ANEMIA)

In myelophthisic anemia the medullary cavities are invaded or occupied by tissues incapable of performing the activities of the displaced marrow The condition differs from aplastic anemia in that there is no expectancy of any resumption of erythrogenesis The prognosis is ominous and at best the patient is maintained in status quo

Organic displacement of bone marrow is observed in the following clinical conditions

Osteopetrosis (Albers Schonberg or Marble Bone Disease) (p 2879) Osteosclerosis or Myelofibrosis as in Polycythemia Vera (p 1093) Carcinomatosis (p 577) Leukemia (p 1100) Multiple Myeloma (p 1126) Hodg

of the mucous membrane and spasm or web like formations in the esophagus Except for hypochromia and microcytosis the hemogram is normal

Treatment—Treatment is effectively carried out by the administration of iron and supplementary vitamins particularly B complex Substitution therapy with hydrochloric acid is advisable Excessive menstrual bleeding may be curbed by injections of androgen (p 2401) or by roentgen therapy

ANEMIAS DUE TO INTRINSIC DEFECTS OF BONE MARROW

Anemias due to intrinsic bone marrow defects present an ominous prognosis since all the processes of erythrogenesis and myelopoiesis are disturbed The more hopeful *aplastic anemias* result from idiopathic toxic and infectious causes With the *myelophthisic anemias* due to organic replacement of bone marrow the prognosis is hopeless and little can be done other than to attempt to keep the patient alive by repeated transfusions

APLASTIC ANEMIA (HYPOPLASTIC ANEMIA AREGENERATIVE ANEMIA)

A variety of etiologic agents may produce the symptom complex of aplastic anemia Essentially it consists of a severe normochromic anemia leukopenia a relative lymphocytosis and a thrombocytopenia The bone marrow in the classical form is made up of yellow fatty hypocellular tissue In a few scattered areas small foci of normal hematopoietic tissue are seen All gradations from hypocellular fatty marrow to active appearing hyperplastic bone marrow may be observed

Etiology—Aplastic anemia results from idiopathic toxic or infectious causes

Idiopathic Aplastic Anemia—Idiopathic examples of aplastic anemia are seen in children young adults and older patients In the young it is likely that the marrow is congenitally deficient or it may be destroyed by some unknown toxic agency In the older group in addition to these possible etiologic factors there may be an element of liver extract deficiency

The idiopathic examples of aplastic anemia tend to run a chronic course Often the disturbance is punctuated with severe hemorrhages In the more favorable instances spontaneous remissions are observed but they are usually transitory

Aplastic Anemias Due to Chemical Agencies—Aplastic anemia is produced by chemical agencies *In industry* the syndrome is most frequently caused by benzol derivatives and radium The occupations that are apt to cause anemia from exposure to benzol derivatives include those that deal with rubber canning photography painting leather and printing In these the toxic agent enters the body by inhalation there is considerable variation in the predisposition to the affliction

In medicine this complication follows radiation therapy tridione the administration of arsenicals gold sulfonamides and dinitrophenol The disturbance may also follow exposure to *chemicals* in hair dyes and volatile insecticides

Although the aplastic anemias of chemical origin are apt to run an acute course their prognosis offers some hope of recovery if the toxic cause is recognized and removed

Aplastic Anemia Due to Infection—In long standing chronic or overwhelming acute infections an aplastic anemia may be observed

Polycythemia Vera (Vaquez Osler Disease Erythremia Chronic Erythremia)

Polycythemia vera is a chronic disease of insidious onset affecting males and females of middle and advanced age

Clinical Manifestations —The clinical manifestations of polycythemia vera are variable and most patients suffer little or no consequence for long periods of time Some of the afflicted are told by friends that their complexion is too ruddy Others note the gradual onset and progression of giddiness dizziness weakness throbbing headache tremors intermittent claudication and paresthesias such as severe burning and tingling of the feet and hands which are most evident in hot weather

The onset may be predominantly digestive with symptoms of peptic ulcer vague but persistent nausea constipation gastric fullness or occasional vomiting Some patients exhibit hemorrhagic manifestations such as epistaxis melena bleeding gums or hemorrhage following operation for an unrelated condition At times a dragging heaviness or an episode of left upper quadrant pain ushers in the disease Less often a major thrombotic accident involving cerebral coronary portal renal mesenteric or peripheral vessels is the initial accident

Physical Examination —The patient with polycythemia vera appears misleadingly healthy The color is ruddy and the cheeks seem to bloom With closer scrutiny however it is apparent that the glow of health is tinged with a cyanotic element the mucous membranes are brick red the patient is usually somewhat thin and tolerates hot weather poorly so that exacerbations occur during the summer months Peculiar erythematous pruritic skin ailments are frequent the fundus oculi reveals marked dilatation of the veins occasional hemorrhages and swelling of the optic disks Heart and lungs show no abnormalities and in most instances the blood pressure is normal but in *Geisbock s syndrome* hypertension without splenomegaly is observed

The *spleen* is often palpable several finger breadths below the costal margin the liver may be enlarged There may be considerable variation in the state of the *peripheral arteries* These vessels may all be patent with normal oscillometric readings even when symptoms are severe At other times the pulsations are poor or absent when there are no subjective complaints It is unusual for gangrene to occur despite peripheral vascular thrombosis since the collateral circulation is efficient The fingers and toes often are clubbed gouty tophi develop as the result of the hyperuricemia

Hematologic Findings —The usual *red blood count* in this disease is about 9 000 000 but as many as 14 000 000 cells per cubic centimeter may be present The *hemoglobin* is often elevated to 120 per cent though values as high as 195 per cent may occur The *color index* is usually less than 1 and as a result of considerable blood letting it may be as low as 0 6 As a rule a slight leukocytosis and normal or elevated platelet counts are observed

The other important findings include an increase in the *hematocrit* reading beyond 55 per cent and marked increases in total *blood volume* and *red cell mass* The *blood uric acid* level may be elevated but *blood*

kin s Disease (p 1138) Gaucher s Disease (p 1133) Nieman Pick disease (p 1134) Hand Christian Schuller's Disease (p 1137)

Clinical Manifestations—Besides the symptoms of the underlying disease myelophthisic anemias produce striking changes in the hemogram The anemia may be normochromic or macrocytic with varying numbers of normoblasts and erythroblasts The leukocytes are usually depressed or normal but may be elevated to the point of resembling a leukemia (p 1100) Under the latter circumstance the spleen undergoes a myeloid hyperplasia *and becomes huge* (*Agnogenic myeloid metaplasia*) Myelocytes and myeloblasts appear in the peripheral blood and the confused situation is only clarified by study of the sternal marrow

The thrombocytopenia may be so extreme as to cause bleeding episodes The extramedullary hematopoietic activities of the liver and spleen produce considerable enlargement of both organs

Treatment—The treatment of myelophthisic anemia consists of repeated *blood transfusions* None of the fundamental lesions is capable of amelioration Splenectomy which removes a major hematopoietic center is contra indicated

POLYCYTHEMIA

An increase in the number of red blood cells per unit volume of blood may be *relative* or *absolute* The latter is most often symptomatic and only rarely constitutes an idiopathic clinical entity

RELATIVE POLYCYTHEMIA

A relative polycythemia exists when there is a transient decrease in plasma volume The *hemoconcentration* is reflected by an apparent increase in the red blood count Such a state results from marked fluid restriction excessive loss of fluid electrolyte imbalances or redistributions of fluid Relative polycythemia occurs clinically after vomiting sweating or diarrhea in diabetic ketosis with shock from any cause with burns and in the crises of adrenal cortical insufficiency

SYMPTOMATIC POLYCYTHEMIA

Symptomatic polycythemia (*erythrocytosis*) is observed in conditions in which a known cause exists for a true increase in the red blood count Usually there is *deficient oxygen saturation* of the arterial blood and a compensatory increase in the numbers of the oxygen carriers

The commoner clinical causes are the *congenital heart anomalies* with a right to left shunt *acquired heart diseases* such as mitral stenosis with chronic pulmonary hypertension *chronic pulmonary disease* (emphysema pulmonary fibrosis and silicosis) *sulf or methemoglobinemia and carbon monoxide intoxication* in which the oxygen capacity of the blood is diminished ascent and prolonged residence at *high altitudes* resulting in a diminution in the partial pressure of oxygen

The cause of symptomatic polycythemia is recognized by physical examination and spectroscopic investigation of the blood *Treatment* is directed at the provocative mechanism

platelets Treatment is checked repeatedly since the development of a leukopenia contraindicates further exposure Roentgen therapy may induce long periods of remission lasting months or years during which time no further treatment is required Exposures are given systematically to the various bones or preferably by the *spray technic* to the entire body

Radioactive phosphorus (P 32) may prove superior to roentgen therapy in polycythemia vera Intravenous injections exhibit their effects on the cells of the bone marrow without the production of radiation sickness The technic is simple toxic symptoms are infrequent and mild radioactivity gradually disappears and retreatments can be given when indicated As in other forms of therapy the complications of myelophthisic anemia and leukemia may be encountered

Benzol Arsenic and Splenectomy—The use of *benzol* as a bone marrow depressant and of *splenectomy* can only be condemned Good results have followed the administration of *Fowler's solution* (Liquor of Sodium Arsenite) in gradually increasing dosage to the point of intolerance Lack of uniform response and frequent toxic manifestations militate against wider use of this remedy Special diets of low iron content are troublesome and yield no benefit

oxygen saturation is normal in contrast to the findings in symptomatic polycythemia

Diagnosis —The diagnosis of polycythemia requires red cell counts hemoglobin determinations and hematocrit readings The possible presence of a relative or symptomatic erythrocytosis is established by demonstration of the more basic abnormalities

Course —The course of polycythemia vera is variable Often a decade passes without subjective manifestations the attention of patient and practitioner may be attracted by an associated phenomenon such as an *unexplained hemorrhage* following an incidental surgical experience an attack of *gout* resulting from the increase in uric acid metabolism that characterizes the disease, or *peptic ulceration* which occurs frequently

In a spent polycythemia the disease terminates in a severe anemic state as a result of fibrosis of the bone marrow (p 1091) It may progress to a *myeloid leukemia* (erythroleukemia) due to overgrowth of the leukopoietic elements of the greatly hyperactive marrow Occasionally the manifestations of a *cirrhosis of the liver* are encountered with chronic portal hepatic or caval vein obstructions due to thrombosis Patients with polycythemia must not be subjected to surgery except as an urgent necessity and should not be exposed to any procedure likely to result in thrombosis such as injection treatments for hemorrhoids or varicose veins

Treatment —The seemingly purposeless increases in blood volume red cell mass red blood count and blood viscosity require reduction since these abnormalities are the causes of the patient s complaints Patients are made more comfortable and their lives are prolonged by careful therapy

Phlebotomy —Phlebotomy or *venesection* (p 853) is an effective safe and logical form of therapy At each blood letting from 300 to 650 cc of blood are removed until the hematocrit readings are consistently below 48 to 50 per cent The procedure usually relieves the symptoms reduces *the likelihood of complications and may usher in a remission of several* months duration

Phenylhydrazine —The chemical treatment of polycythemia utilizes destruction of the excessive red blood cells by the use of hemolytic toxins such as *phenylhydrazine hydrochloride* or preferably *acetylphenylhydrazine (pyrodine)* These drugs destroy large numbers of red blood cells but their activity is cumulative they have undesirable and insidious side effects on *liver marrow and stomach and they promote vascular thrombosis*

Pyrodine (p 1049) is administered daily in 100 mg (1 ⅓ grains) capsules The patient is observed carefully for the first evidences of hemolysis at which time the drug is stopped The hemolytic effect is manifest first by a leukocytosis later by icterus and a precipitate fall of the red blood count Not more than 1 gm (15 grains) should be given in the first course and a weekly maintenance dose of 100 to 300 mg (1⅔ to 5 grains) usually is required to keep the red blood count down to a satisfactory level We are among those who greatly fear to use hemolytic drugs and prefer the more cumbersome method of frequent blood lettings

Roentgen Therapy —Radiation to the bones with the exception of the skull and pelvis inhibits the greatly hyperactive bone marrow This therapy is particularly indicated with marked increases in the leukocytes or

acutely with *dysphagia* or an insidious onset with lassitude may be the presenting complaint There is variation in the development of symptoms The acute course is marked by prostration and high temperature Large grey necrotic ulcerations appear in the mouth throat or any other of the

DIFFERENTIAL DIAGNOSIS OF

Leukocytosis (Neutrocytosis Neutrophilia)

Neutrocytosis is associated with alterations in the character as well as the quantity of the cells With excessive stimulation of bone marrow immature forms appear in the circulating blood. These are recognized by the absence of nuclear segmentation and the presence of but two lobes in young or juvenile forms Preponderance of immature cells is termed a shift to the left whereas conversely an increase in four or five-lobed neutrocytes is a shift to the right In addition to nuclear changes basophilic or toxic granulation frequently appears in intense neutrocytosis This phenomenon bears some relationship to the severity of the stimulus eliciting the neutrocytic response and is of value prognostically and as an index of the efficacy of therapy

CAUSE	DIAGNOSTIC FEATURES
Coccal Infection	With staphylococci streptococci pneumococci gonococci and meningococci Make bacteriologic studies (p 54)
Rickettsial Disease	Typhus and Rocky Mountain Spotted Fevers *(p 366) Note eruption and get serology* (p 59)
Virus Infection	Rabies poliomyelitis smallpox, chickenpox and herpes zoster Note eruption (p 17[illegible])
Fungous Infection	Particularly actinomycosis (p 483) Get smear
Aseptic Destruction of Tissue	As in acute cardiac infarction from recent coronary artery thrombosis (p 983) Get ECG
Acute Hemolysis	As in acute hemolytic anemia (p 1060)
Acute Hemorrhage	Due to stimulation of bone marrow
Muscular Activity	Following convulsions and delivery
Postoperative	*For 24 or 48 hours following operation in the absence of infection*
Chemical	From the ingestion of irritating chemicals such as turpentine
Toxic	In diabetic acidosis, gout, and uremia With eclampsia intestinal obstruction and extensive burns in the absence of infection
Parenteral Injections of Foreign Protein	Such as milk or typhoid vaccine
Diseases of the Blood Forming Organs •	In myeloid leukemia Hodgkin s disease infectious mononucleosis and polycythemia vera Get hemogram marrow smear and biopsy (p 1043)

body orifices or intestinal tract The lesions resemble the ulcerations of *fusospirochetosis leukemia* or *infectious mononucleosis* Erythematous skin lesions appear and often become gangrenous and necrotic Spreads and cultures of the ulcerated lesions reveal great variations in the bacterial flora but *fusospirochetes* are most often present As the result of sepsis

CHAPTER 51

CONDITIONS DUE TO DISTURBANCES OF LEUKOCYTES AND THROMBOCYTES

LEUKOCYTOSIS

LEUKOCYTOSIS exists when the numbers of the circulating white cells exceed 10 000 per cu mm The commonest variety of leukocytosis is caused by an increase in neutrophils and constitutes a neutrocytosis or neutrophilia Less frequently the practitioner encounters basophilia eosinophilia (p 542) lymphocytosis (p 1098) and monocytosis (p 1099)

AGRANULOCYTOSIS (MALIGNANT NEUTROPENIA GRANULOCYTOPENIA AGRANULOCYTIC ANGINA)

Agranulocytosis is a symptom complex that has become fairly common since the widespread and indiscriminate use of *aminopyrine* and its derivatives

Etiology —Most of the examples of agranulocytosis are due to exposure to a toxic substance usually aminopyrine most often taken with other *analgesics or sedative drugs in patent medicines The symptoms may* begin after one a few or many doses of the agent Other drugs that have produced the same syndrome include *dinitrophenol gold arsenobenzol sulfonamides tridione* the *barbiturates* and *thio uracil*

LIST OF AMERICAN PROPRIETARY PREPARATIONS THAT DID OR DO CONTAIN AMIDOPYRINE

Allonal	Antabs	Gardan	Neurolyne
Alphebin		*Gynalgos*	*Nod*
Amarbital	Benzedo Compound		
Amidol	Buramid	Hexin	Optalidon
Amido neonal	Burb-Amid		
Amidomine		*Ipral Aminopyrine*	*Peralga*
Amidophen	Cibalgine		Phenamidal
Amidos	Cinchopyrine	Kalms	Phen Amidol
Amidotal Compound	Compral		Phenopyrine
Amifeine	Cronal	Lumodrin	Pyramidon
Aminal			Pyraminal
Amnalgia	*Dymen*	*Midol*	
Am Phen Al	Dysco	Mylin	Sequit
Ampydin			
Amytal Compounds	En Med	Neonal Compound	Yeast—Vite

Clinical Manifestations —Agranulocytosis occurs most often in middle aged females and person included in the *medical personnel It may start*

acutely with *dysphagia* or an insidious onset with lassitude may be the presenting complaint There is variation in the development of symptoms The acute course is marked by prostration and high temperature Large grey necrotic ulcerations appear in the mouth throat or any other of the

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Neutrocytosis is associated with alterations in the character as well as the quantity of the cells With excessive stimulation of bone marrow immature forms appear in the circulating blood These are recognized by the absence of nuclear segmentation and the presence of but two lobes in young or juvenile forms Preponderance of immature cells is termed a shift to the left whereas conversely an increase in four or five lobed neutrocytes is a shift to the right In addition to nuclear change basophilic or toxic granulation frequently appears in intense neutrocytosis This phenomenon bears some relationship to the severity of the stimulus eliciting the neutrocytic response and is of value prognostically and as an index of the efficacy of therapy

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Virus Infection	Rabies poliomyelitis smallpox chickenpox and herpes zoster Note eruption (p 172)
Fungus Infection	Particularly actinomycosis (p 499) Get smear
Aseptic Destruction of Tissue	As in acute cardiac infarction from recent coronary artery thrombosis (p 983) Get ECG
Acute Hemolysis	As in acute hemolytic anemia (p 1060)
Acute Hemorrhage	Due to stimulation of bone marrow
Muscular Activity	Following convulsions and delivery
Postoperative	For 24 or 48 hours following operation in the absence of infection
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Parenteral Injections of Foreign Protein	Such as milk or typhoid vaccine
Diseases of the Blood Forming Organs	In myeloid leukemia Hodgkin's disease infectious mononucleosis and polycythemia vera Get hemogram, marrow smear and biopsy (p 1043)

body orifices or intestinal tract The lesions resemble the ulcerations of *fusospirochetosis leukemia* or *infectious mononucleosis* Erythematous skin lesions appear and often become gangrenous and necrotic Spreads and cultures of the ulcerated lesions reveal great variations in the bacterial flora but *fusospirochetes* are most often present As the result of sepsis

and overwhelming toxicity albumin and formed elements appear in the urine and jaundice may develop

Course —In fatal instances signs of pulmonary involvement or a terminal sepsis make their appearance The fever continues hectic and death

DIFFERENTIAL DIAGNOSIS OF

Basophilia

Basophilia is infrequently seen and the significance of the finding is at present unknown

CAUSE	DIAGNOSTIC FEATURES
Myeloid Leukemia	Cells occasionally basophilic or resembling mast cells Get marrow smear (p 1043)
Hepatic Disturbances	*Such as cirrhosis of the liver and chronic* hemolytic icterus
Infectious	In smallpox and chickenpox Note eruption
Disturbances of the Blood	In polycythemia vera Hodgkin s disease secondary anemias and following splenectomy

DIFFERENTIAL DIAGNOSIS OF

Lymphocytosis

A lymphocytosis is normal after the tenth neonatal day and during the first year or two of life The percentage of the mononuclear cells may rise to 60 or 70 until the third year when the neutrophils gain

CAUSE	DIAGNOSTIC FEATURES
Acute Infections	Pertussis mumps rubella congenital and secondary syphilis typhoid fever chronic malaria chickenpox and smallpox Note eruption Get blood smears serology and bacteriologic data (p 54)
Infectious Mononucleosis	Increased total and differential count of peculiar mononuclear lymphoid cells (p 466) Positive heterophile reaction and false positive Wassermann tests (p 337)
Leukemia	In chronic and acute lymphatic varieties as well as leukosarcoma Get marrow smear (p 1043)
Hyperthyroidism	In Graves disease with elevation of B M R Note therapeutic response to iodine (p 1213)
Following Radiation	With x ray or radium (p 3796)

usually follows within a week Almost any organism most often a hemolytic streptococcus or a pneumococcus may be recovered from the blood stream

With some patients the disease progresses slowly with low grade fever and relatively slight clinical discomfort Others less fortunate progress

inexorably and after one or more weeks develop the fullblown clinical state

Laboratory Findings—The peripheral blood picture of agranulocytosis is characteristic There is a pronounced and progressive diminution in the *white blood count* to 500 or fewer leukocytes all or most of which are lymphocytes The red blood cells and platelets are present in normal or diminished numbers An anemia is often associated when the etiological agent is arsenobenzol sulfonamide or gold The *bone marrow* obtained by puncture may be markedly aplastic as regards the leukopo etic elements it may appear fairly normal or it may contain large numbers of very immature leukopoietic cells without mature granulocytes These variations depend in part at least on the stage of the disease when the examination is performed Occasionally it is difficult to differentiate the marrow changes of an agranulocytosis from those of an acute leukemia and under these circumstances the expert hematologist is consulted

DIFFERENTIAL DIAGNOSIS OF

Monocytosis

Monocytes normally constitute 5 to 10 per cent of the total number of circulating white cells

CAUSE	DIAGNOSTIC FEATURES
Infections	Tuberculosis subacute bacterial endocarditis leishmaniasis typhoid fever typhus fever brucellosis malaria trypanosomiasis Get blood culture serology blood smears and skin tests (p 59)
Infectious Mononucleosis	See Lymphocyto is (p 1098)
Diseases of Blood Forming Organs	In monocytic leukemia Hodgkin s disease agranulocytosis Gaucher s disease Niemann Pick syndrome and essential xanthomatosis Get marrow smear and biopsy (p 1043)

Prognosis—While agranulocytosis is a severe and often fatal affliction favorable prognostic signs are the presence of more than 4 per cent mono cytes an eosinophilia in the peripheral blood cessation of fall and increase in the numbers of leukocytes the appearance of nonsegmented neutro phils and the presence of a cellular leukopoietic bone marrow

Treatment—The first and most important step in therapy is to cease contact with the offending etiologic agent The patient is kept in bed since the local ulcerating lesions require vigilant nursing care They are fre quently washed with saline or sodium perborate and may be painted with 1 per cent aqueous gentian violet Sedatives analgesics and most other drugs are avoided if possible to prevent further injury to the leukocytes Opium derivatives have a negligible threat

Small frequent *blood transfusions* during the acute stage are of in dubitable benefit Fresh blood is superior to stored bank blood for this purpose Fifteen to thirty five injectible units of refined *liver extract* or more of the crude extract are often used daily to advantage

Derivatives of Nucleic Acid—As the result of experimental investiga

tions which disclose leukocyte stimulation by nucleic acid and its derivatives injections of *sodium nucleinate guanine hydrochloride adenine sulfite* and *pentnucleotides* have been introduced into clinical therapeutics Of these pentnucleotide is commercially available and its use by intramuscular injection in doses of 0 5 to 0 8 gm (5 to 10 cc) is regarded as the most specific and potentially effective myelopoietic stimulus' The injections are given two hours after meals to avoid unpleasant reactions which include substernal constriction headache nausea and chilling The pentnucleotide injections are continued until improvement in the blood count is observed

Yellow Bone Marrow—A yellow marrow concentrate derived from cattle has been prepared in capsules of 0 22 gm (3⅓ grains) Advocates of this preparation suggest the oral use of 50 to 200 capsules daily until improvement is noted and then the dose is reduced to 25 to 50 capsules We have no experience with this preparation but its administration can do no harm and is worthy of trial

Roentgen Therapy—Despite the fact that roentgen therapy may produce leukopenia daily exposure with ⅟₀ skin erythema doses is advocated in the management of granulocytopenia We are fearful of this form of treatment and prefer placing reliance on spontaneous improvement or the combination of transfusions and injections of pentnucleotide

Penicillin—The introduction of prompt and massive penicillin therapy (p 106) has revolutionized the management of agranulocytic angina Results of treatment have completely altered the prognosis

GRANULOCYTOPENIAS

Besides agranulocytosis usually of definitely toxic origin granulocytopenias of idiopathic causation have been described as clinical rarities

Primary Splenic Granulocytopenia—Primary splenic granulocytopenia has been observed as an acute subacute or chronic affliction The presenting manifestation is a more or less specific destruction of the circulating granulocytes without demonstrable cause The spleen is usually but not invariably enlarged and other findings are conspicuously absent or inconstant

Treatment follows the principles established in agranulocytosis (p 1096) When improvement fails to occur splenectomy (p 1053) is considered and may be followed by complete recovery

Felty s Syndrome—The triad of leukopenia splenomegaly and chronic infectious polyarthritis constitutes a distinct clinical entity, described by Felty Its recognition is of importance because of the favorable effects of splenectomy (p 1053)

INFECTIOUS MONONUCLEOSIS

See *Generalized Infections* (p 466)

LEUKEMIA

Leukemia is a disease of unknown etiology It is characterized by an abnormal proliferation of the leukopoietic tissues and usually results in an increase in the number of the circulating leukocytes

The leukemias are classified as acute subacute or chronic depending on

the rapidity of the clinical course They are further subdivided according to the predominating cells as lymphoblastic myeloblastic and monoblastic forms According to another and preferable terminology leukemias are designated as *leukocythemic* with an increase in the numbers of circulating leukocytes and *leukopenic* with normal or decreased numbers of circulating leukocytes

Etiology —Present medical knowledge does not throw light on the etiology and pathogenesis of leukemia There are certain definite predisposing factors such as exposure to aniline coal tars benzol and radioactive substances We have been impressed with the disproportionately large number of roentgenologists who have succumbed to the disease

Experimental investigations are suggestive of infectious and neoplastic factors in the production of the disturbance Leukemia is transmissible in fowls by means of cell free filtrates although the relationship of this disorder to human leukemia is questionable Extracts of urine from leukemic patients have been reported to produce leukemia when injected into animals Relative to the metabolism of vitamin A and fractions of vitamin B complex leukemia and neoplastic disorders re pond similarly

Age and Sex Incidence.—The acute leukemias are usually observed in the first second and third decades of life Subacute and chronic varieties are encountered in the middle years The sexes seem to be equally affected in chronic leukemia but the acute variety is more often found in males Leukemia seems not to be a familial disease but it has been described in twins

The Clinical Manifestations of Acute Leukemia —The acute leukemias have an abrupt onset with fever extreme prostration and lassitude Presenting manifestations may be many and varied They include the hemorrhagic tendency buccopharyngeal lesions enlargement of lymph nodes and spleen respiratory symptoms due to pressure from the mediastinal glands or neurological manifestations resulting from leukemic infiltrations or hemorrhages in the structures of the nervous system These last are most confusing and may simulate an encephalitis a transverse myelitis a meningitis or the Waterhouse Friderichsen syndrome of acute adrenal insufficiency Cranial nerve palsies are seen and diffuse flame shaped hemorrhages appear in the fundus Detachment of the retina often occurs blindness and visual scotomas are encountered deafness follows hemorrhage into the ear

The prognosis of acute leukemia is hopeless The duration varies from a few days to a few months and the majority of patients survive only two to four weeks from the onset of symptoms

Buccopharyngeal Type—The buccopharyngeal type of onset is found most commonly in the acute *monocytic leukemias* The gums buccal mucosa pharynx and tonsils are spongy swollen hemorrhagic ulcerated and later necrotic with superimposed secondary infection usually due to *fuso spirochetes* Dysphagia is common and edema of the pharynx uvula and epiglottis may be so extreme as to necessitate tracheotomy (p 3958) Often the localization of the inflammatory process leads the patient first to consult a *dentist* or a *rhinolaryngologist* Often the conditions are erroneously considered as pyorrhea gingivitis acute tonsillitis Vincent s angina or trench mouth

The Lymphatic Variety—The lymphatic variety is usually a manifes

tions which disclose leukocyte stimulation by nucleic acid and its derivatives injections of *sodium nucleinate guanine hydrochloride adenine sulfite* and *pentnucleotides* have been introduced into clinical therapeutics Of these pentnucleotide is commercially available and its use by intramuscular injection in doses of 0 5 to 0 8 gm (5 to 10 cc) is regarded as the most specific and potentially effective myelopoietic stimulus' The injections are given two hours after meals to avoid unpleasant reactions which include substernal constriction headache nausea and chilling The pentnucleotide injections are continued until improvement in the blood count is observed

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Felty s Syndrome—The triad of leukopenia splenomegaly and chronic infectious polyarthritis constitutes a distinct clinical entity described by Felty Its recognition is of importance because of the favorable effects of splenectomy (p 1053)

INFECTIOUS MONONUCLEOSIS

See *Generalized Infections* (p 466)

LEUKEMIA

Leukemia is a disease of unknown etiology It is characterized by an abnormal proliferation of the *leukopoietic* tissues and usually results in an increase in the number of the circulating leukocytes

The leukemias are classified as acute subacute or chronic depending on

may be observed and the white blood cell counts may vary from 200 to 250 000

Thrombocytopenia is usual and may be of such severe grade that purpuric manifestations are the most prominent symptoms Platelet counts as low as 5000 have been seen Due to the low platelet counts the *bleeding time* is usually prolonged and *clot retraction* may be slight or absent The *coagulation time* may be normal or prolonged *Anemia* usually occurs if the patient survives for more than a week or two The hemoglobin level may fall to as low as 20 per cent and the red cells are depressed to a corresponding level The anemia is usually of the normochromic and normocytic variety Occasionally young red blood cells are found in the blood smear Normoblasts erythroblasts and polychromatophilia are a manifestation of bone marrow activity and an attempt on the part of the body to restore a normal equilibrium A hemolytic anemia with reticulocytosis and increased urobilinogen output in the urine and stool is an occasional finding

The Hemogram in Chronic Leukemia —In chronic leukemia leukocytosis or leukopenia may be present the counts varying from 1000 to 500 000 or over The lymphatic type is more commonly leukopenic The white blood cells show a variety of forms in the myeloid types and a smear of the blood is similar in appearance to that of bone marrow Myeloblasts myelocytes immature and mature leukocyte forms normoblasts megakaryocytes megakaryocytic fragments and giant platelets are not uncommonly seen

In chronic *lymphatic* leukemia there is the dull monotonous regularity of small round lymphocytes These cells are apparently normal but an occasional lymphoblast or smudge cell is found In chronic *monocytic* leukemia the predominating cell is the mature monocyte and only an occasional monoblast is seen The platelets are usually normal or increased in number In chronic *myeloid* leukemia a thrombocytosis of over a million is the cause of frequent episodes of thrombosis

The anemia may be quite severe as the chronic leukemia progresses It is usually normochromic in type and immature red cells may be present Anisocytosis is common polychromatophilia reticulocytosis and basophilic stippling occasionally occur

The Bone Marrow in the Leukemias —The spreads of marrow obtained by sternal aspiration leave no doubt as to the diagnosis of acute and chronic leukemia The marrow is usually hyperplastic and in acute leukemia the immature cell types predominate Over 90 per cent of the marrow cells are in the blast stage and these cells crowd out other cell forms resulting in the peripheral blood picture of leukocytosis anemia and thrombocytopenia

In chronic leukemias sternal aspiration is of greatest value in the leukopenic forms when the diagnosis is in doubt In *chronic myeloid leukemia* myeloblasts myelocytes metamyelocytes and juvenile polymorphonuclear cells predominate in *chronic lymphatic leukemia* the bone marrow shows lymphocytes in excess of 30 per cent In *aleukemic leukemia* the expert hematologist rarely fails to recognize the cytological abnormalities despite the misleading appearance of the peripheral blood See p.

Atypical Leukemias —In addition to aleukemic l

tation of an acute *lymphoblastic leukemia* There is generalized glandular enlargement and the spleen is palpable 3 to 4 cm below the costal margin The cervical glands may be greatly enlarged in both monocytic and lymphoblastic varieties

The Hemorrhagic Type —The hemorrhagic type is found in acute *myeloblastic leukemias* Nosebleeds ecchymoses bleeding gums diffuse purpura and hemorrhage from body orifices call attention to the affliction

The Clinical Manifestations of Chronic Leukemia —Chronic leukemia undoubtedly remains asymptomatic for long periods of time The diagnosis is often established by a routine blood count and years may pass before the patient notes any related discomforts On the other hand we have observed patients who complained of overwhelming fatigue for a considerable period of time before evidences of the leukemia were demonstrable in the peripheral blood

The commonest complaints are weakness anorexia easy fatigability *marked weight loss extreme perspiration and nervousness Fever is* uncommonly observed but may be of the septic variety as seen in Hodgkin s disease (p 1138)

Lymphadenopathy —Glandular enlargement is usually extreme in chronic lymphatic leukemia and less often in chronic myelogenous varieties The glands are firm and movable They may become confluent and form a collar about the neck as seen in *Hodgkin s disease* and *lymphosarcoma* Occasionally the *lacrimal glands* are involved as in *Mikulicz s syndrome* (p 1709) The lymphadenopathy rarely causes pain but disturbances arise as the result of pressure Thus cough and dyspnea are due to pharyngeal or mediastinal lymphadenopathy enlargement of the abdominal glands may cause obstructive jaundice intestinal obstruction or acute irritation of the peritoneum suggesting the presence of an acute surgical condition

Splenomegaly and Other Disturbances —Splenic enlargement is extreme in the chronic myelogenous and monocytic varieties The organ usually is firm the notch is easily palpable but there is no tenderness unless infarcts produce perisplenitis

The *liver* is usually enlarged firm and tender Jaundice is rarely encountered unless there is lymphatic obstruction to the main biliary radicles *Gastro intestinal symptoms* such as anorexia nausea vomiting distention and flatulence are common features of the disease

Priapism (p 2411) may be a first sign of leukemia due to infiltration of the corpora cavernosa Hemorrhagic manifestations are uncommon in chronic leukemia though nasal hemorrhages occasionally occur Specific *dermatoses* often call the condition to the attention of the physician There may be leukemic infiltrations of the skin or nonspecific afflictions such as pustules papules hemorrhagic manifestations or herpes *Bone tenderness* over the lower sternum is a particular feature of chronic leukemia and probably results from disturbance of the marrow

The Hemogram in Acute Leukemia —In acute leukemia the leukocytes are usually of a *uniform and immature* type and *leukocytosis* is the rule The majority of the cells are *myeloblasts lymphoblasts* or *monoblasts* There may be great difficulty in differentiating the cell types but this is the province of the expert Instead of leukocytosis an extreme *leukopenia*

lar manifestations are encountered in the leukemias Basophilocytic eosinophilocytic and clasmatocytic varieties are described

Chloroma—Chloroma is a type of myeloblastic leukemia characterized by the occurrence of *localized tumors* in the skull ribs and small bones of the body The course of the disease is similar to that of acute leukemia

The blood examination reveals a myeloblastic leukemic picture and punctures of the isolated tumorlike masses show myeloblastic infiltrations The tumorlike masses are greenish in color due to the presence of a porphyrin like substance

Megakaryocytic Leukemia—A megakaryocytic leukemia is said to exist when the bone marrow spleen liver and other organs contain many megakaryocytes The platelet level in the peripheral blood may be high Bizarre giant forms or fragments of megakaryocytes are observed These findings have been encountered in myeloid leukemia polycythemia vera (p 1093) osteosclerosis (p 2879) myelofibrosis (p 1091) and rare forms of congestive splenomegaly (p 1131)

Plasma Cell Leukemia—Plasma cell leukemia occurs as a phase of *multiple myeloma* (p 1126) but it may be noted without bone changes The plasma cell predominates in the circulating blood and leukocytosis is usual

Leukosarcoma—Leukosarcoma refers to examples of lymphosarcoma in which a leukemic blood picture is present and leukosarcoma cells are found in the circulating blood This condition is probably midway between leukemia and lymphosarcoma and represents a transition phase similar to the giant follicle lymphoblastoma later discussed (p 1137) Glandular enlargement is common with a leukocytosis of 100 000 to 200 000 per cubic centimeter

Erythroleukemia (*Acute Erythremia*)—Erythroleukemia or acute erythremia is a disease characterized by weakness fever splenomegaly and hepatomegaly The onset is abrupt and the course is rapid There is no leukocytosis and the blood picture shows numerous immature red cells myeloblasts and myelocytes The disease is similar to an acute leukemia except for the proliferation of the erythroid tissue The term erythroleukemia is sometimes used to denote myeloid leukemia in polycythemia vera

Diagnosis—The diagnosis of leukemia should be deferred by the practitioner until he has submitted blood and marrow specimens to the expert hematologist Two serious pitfalls one positive and the other negative await the unwary The error of failing to recognize a leukemia in the aleukemic phase is less serious but that of definitively diagnosing a fatal leukemia on the basis of the blood findings of a benign acute mononucleosis is unforgivable See p 466

In the *preleukemic* and *aleukemic* varieties of leukemia the peripheral blood may show nothing pathognomonic at a time when the expert clearly recognizes the ominous nature of the disturbance by his study of spreads obtained by sternal puncture

Infectious mononucleosis has often been mistaken for leukemia In all likelihood the reported recoveries and cures of leukemia refer to patients in whom the fatal disease never existed Infectious mononucleosis may simulate an acute leukemia in its clinical aspects and peripheral hem

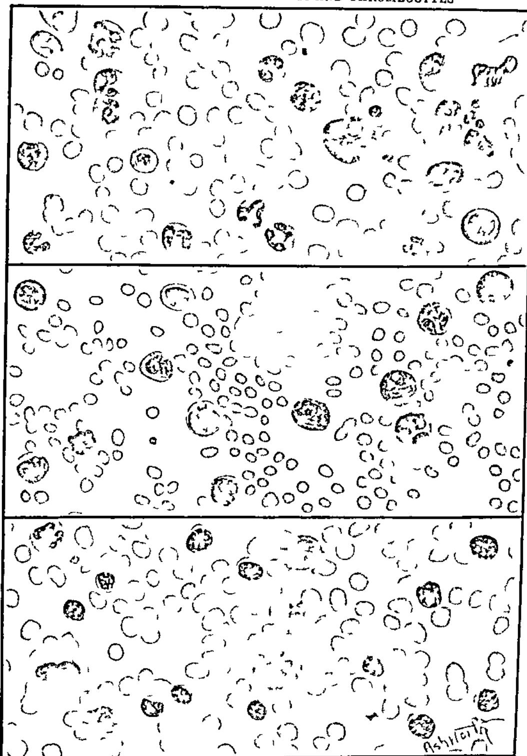


Fig 233—Blood picture in leukemias *Top* Chronic leukemic granulocytic leukemia *Center* Acute granulocytic (myelogenous) leukemia as shown in the peroxidase stain *Lower* Chronic lymphocytic leukemia *

Courtesy of Eli Lilly and Company

given for three days in a dose of 5 drops three times daily It is best administered in orange juice following meals The dose is increased 1 drop daily up to 15 drops three times daily If toxic symptoms appear or if a remission occurs a maintenance dose of 5 to 10 minims three times daily is advised

Iodide—The elevated basal metabolic rate observed most often in chronic lymphatic leukemia produces some of the asthenia and weight loss that characterizes the affliction The administrations of Lugol s Solution as in hyperthyroidism (p 1197) corrects the metabolic disturbances and provides symptomatic relief

Nitrogen Mustards—The use of nitrogen mustards has not added significantly to results of roentgen therapy in acute or chronic leukemias

THROMBOCYTOPENIA

See *Hemorrhagic Diseases* (p 1117)

THROMBOCYTOSIS

See *Peripheral Venous Thrombosis and Embolism* (p 1123)

THROMBASTHENIA

See *Hemorrhagic Diseases* (p 1117)

atological findings The expert however, recognizes the morphological characteristics of the benign mononucleosis his judgment is corroborated by the presence of the positive *heterophile serological test* (p 467) and the benign course of the disease The senior author has learned through bitter experience the error of trusting the judgment of any but an expert in this differential diagnosis The practitioner is urged to recall that (*1*) Infectious mononucleosis is a very common affliction whereas acute leukemia is relatively rare (*2*) spreads and counts of peripheral bloods are indistinguishable except to the expert in the two conditions (*3*) the diagnosis of acute leukemia, a fatal disease can never be made too late (*4*) the hope that the condition is a mononucleosis should be maintained until the opinion of the hematologist is verified by the downhill clinical course

Treatment—The treatment of leukemia is directed at the alleviation of the more distressing symptoms due to glandular enlargement anemia or the increased metabolic rate Patients with asymptomatic chronic leukemia are best treated by skillful neglect until such time as discomforts arise A well balanced high caloric diet is recommended Rest in bed is unnecessary unless fever is present The teeth are examined periodically and necessary extractions are done in a hospital so that hemorrhage which is frequent may be readily controlled A mouth wash of sodium perborate is used and ⅓ strength hydrogen peroxide is efficacious in the presence of fusospirochetoses *Blood transfusions* are useful if the anemia is severe or the asthenia is extreme *Iron* and *liver extract* are of value only in chronic myeloid leukemia *Benzol* although extensively used in Europe is dangerous through its depressant effects on bone marrow

Roentgenotherapy—Roentgenotherapy is advised in chronic leukemia when there is marked glandular enlargement or anemia Exposures are withheld as long as possible since many patients eventually become refractory to therapy Most roentgenotherapists favor small frequent doses of 100 R In chronic lymphatic leukemia treatment of the glands may cause the symptoms to disappear for months while the blood picture becomes relatively normal In chronic myeloid leukemia radiation to the spleen and bones also is indicated Frequent blood examinations are required since therapy must be interrupted if there is an abrupt fall of red or white cells or the platelets

There is no *contraindication* to radiotherapy other than in acute leukemia where it is rarely if ever beneficial Radiation sickness may be prevented and the symptoms are alleviated by large doses of the vitamin B complex

Radioactive Phosphorus—Radioactive phosphorus (P 32) (p 1049) has proved helpful in the treatment of *chronic leukemia* although it is of no value in the fulminating examples of acute leukemia The substance is given intravenously radiation sickness rarely if ever occurs The effects observed are similar to those of other forms of radiotherapy

Arsenic—Arsenic has been used successfully in the treatment of *chronic myeloid leukemia* but is of no avail in the acute leukemias or chronic lymphatic leukemia At times complete remissions follow the use of Liquor of Potassium Arsenitis (*Fowler s Solution*) which may be beneficial when the patient develops refractiveness to radiotherapy Fowler s solution is

THE AGENCIES INVOLVED IN THE CLOTTING OF BLOOD

The agencies involved in the clotting of blood are vitamin K ionized calcium prothrombin thromboplastin fibrinogen and the blood platelets or thrombocytes

Vitamin K.—Vitamin K is a *naphthoquinone derivative* that is widely distributed in the plant kingdom In addition to its exogenous origin it can be manufactured by intestinal bacteria from elementary precursors

Absorption and Function.—Ingested vitamin K reaches the absorbing surface of the small intestines without undergoing any significant change In the presence of *bile salts* it is absorbed with great facility After absorption the vitamin plays an integral role in the *synthesis of prothrombin* by the liver cell It may enter into the structure of prothrombin or function as a catalyst in the process of synthesis

Anti hemophilic Fraction.—Plasma yields a fraction which lowers the coagulation time of hemophiliacs This Fraction I or anti hemophilic fraction is of value in the prevention and control of bleeding

Vitamin K Deficiency.—Vitamin K deficiency may arise from abnormalities in the diet absence of bile salts necessary for its absorption disturbances of the intestinal mucous membrane preventing its absorption or derangement or destruction of the liver cells and a resultant interference with the synthesis of prothrombin See *Hypoprothrombinemia* (p 1111)

While the estimation of vitamin K content is not practicable its deficiency may be hypothecated from measurements of prothrombin time The *treatment* of vitamin K deficiency is by the artificial ingestion of the readily available commercial product (p 630) with or without the simultaneous feeding of bile salts (p 1990)

Ionized Calcium.—The presence of ionized calcium is essential for the conversion of prothrombin to thrombin There are no clinical disturbances in the bleeding mechanism that are due to calcium deficiency or unavailability of ionized calcium

Prothrombin.—Prothrombin synthesized in the liver cells through the agency of vitamin K is the precursor of thrombin Under normal circumstances prothrombin is present in considerable excess in the blood The normal amount may be decreased as low as 20 or 30 per cent before prolongation of the coagulation time occurs and clinical manifestations appear Methods for estimating the prothrombinemia level of the blood are available

Hypoprothrombinemia.—Hypoprothrombinemia is present in all types of vitamin K deficiency It may also exist in diseases of the liver cells since it is here that it is synthesized Certain toxic substances (*dicoumarins*) in some unknown way bring about a lowering of the prothrombin activity of the blood These preparations are used in the treatment of thrombotic disturbances Decreased activity of prothrombin occurs occasionally in polycythemia vera and pernicious anemia

Prothrombin and Antiprothrombin.—The prothrombin of the circulating blood is held in equilibrium by an *antiprothrombin* a substance that is probably identical with *heparin* Theoretically an excess of antiprothrombin may produce a tendency toward bleeding So far as is known this does not occur spontaneously in clinical medicine though the therapeutic administration of preparations of heparin (p 1050) upsets the prothrombin antiprothrombin relationship in favor of the latter substance and are used in the treatment and prevention of *intravascular thrombosis*

Thromboplastin.—Thromboplastin is the substance which converts prothrombin into thrombin The reaction requires the presence of ionized calcium Thromboplastin is liberated by injured tissue and by blood platelets exposed to foreign surfaces So far as is known there are no clinical conditions in which there is a deficiency of tissue thromboplastin Platelet thromboplastin may be lacking in thrombocytopenia, thrombasthenia and hemophilia

Fibrinogen.—Fibrinogen is a plasma soluble protein manufactured in the liver Under the influence of the enzyme thrombin it is converted to the solid fibrin of the clot Measurements of plasma fibrinogen are rarely required in clinical medicine Deficiencies occur as the result of profound liver damage

The Blood Platelets or Thrombocytes.—The blood platelets or thrombocytes are normally present in the circulating blood in the amount of 150 000 to 00 000 per cubic millimeter

Thrombocytopenia and Thrombocytosis.—A decrease in the number to approximately 100 000 or less constitutes a significant *thrombocytopenia* (p 1114) which must be regarded as a possible cause of a hemorrhagic state An increase to 800 000 or 1 000 000 platelets constitutes a *thrombocytosis* (p 1118)

In the mechanism of blood coagulation the thrombocytes probably affect the quality

CHAPTER 52

DISTURBANCES OF BLOOD COAGULATION

THE maintenance of life is dependent upon the ability of the blood to remain fluid in its intravascular existence and to clot when it escapes from the vessels The clinical abnormalities pertinent to the physical state of the blood constitute the hemorrhagic diatheses and instances of intravascular thrombosis

THE HEMORRHAGIC DIATHESES

The hemorrhagic diatheses include a variety of clinical disturbances *which have a common tendency to widespread or systemic bleeding They* are distinguished from local bleedings which occur as the result of some isolated pathologic condition The broader systemic disturbances may be predicated if there are bleedings from several sites although bleeding from a single focus does not exclude the possibility of a widespread derangement The hemorrhagic diatheses may be due to abnormalities of the clotting of the fluid blood and disturbances of the permeability of the capillary walls

Abnormalities in the clotting mechanism are diagnosed mainly by determinations of the prothrombin level of the blood the bleeding time the enumeration of the blood platelets the estimation of the coagulation time and clot retractions These tests are well within the scope of the office laboratory (p 3692)

Disturbances of capillary permeability are usually characterized by normal laboratory findings in the tests of the clotting mechanisms Positive evidence of the source of the difficulty is afforded by capillary fragility tests These may be carried out by making counts of the petechiae in a given *skin surface* area after (1) the application of a tourniquet (Rumpel Leede phenomenon p 628) (2) after pinching the skin or (3) after injecting intracutaneously a small amount of moccasin venom

Disturbances of Blood Platelets
- Essential Thrombocytopenic Purpura
- Symptomatic Thrombocytopenia
- Chronic Hereditary Thrombasthenia
- Thrombocytosis

Fibrinogenopenia and Afibrinogenemia
Hemophilia
Disturbances of Capillary Permeability
- Hereditary Hemorrhagic Telangiectasia (Rendu-Osler Weber Disease)
- Vitamin C Deficiency (Scurvy)
- Hemorrhagic Capillary Toxicosis (Henoch Schonlein's Purpura)

Bleeding of Unknown Cause

Differential Diagnosis.—See Table 76 (p 1112)

HYPOPROTHROMBINEMIA

Prothrombin the precursor of the enzyme thrombin is synthesized in the liver in the presence of an adequate supply of vitamin K Hypoprothrombinemia may be a manifestation of lack of vitamin K or it may represent an inability on the part of the liver to synthesize prothrombin When vitamin K deprivation is the cause of the hypoprothrombinemia the defect can be corrected by oral or parenteral use of the vitamin Prothrombin deficiency of hepatic insufficiency is suggested when the liberal parenteral administration of vitamin K or other naphthoquinone preparations fails to cause a rise in the blood prothrombin level

VITAMIN K DEFICIENCY

Deficiency of vitamin K may occur through (1) a dietary insufficiency (2) interference with absorption as in obstructive jaundice and (3) with insufficient storage reserve as occurs in the hemorrhagic disease of the newborn

Avitaminosis —The wide distribution of vitamin K in dietary ingredients its low daily requirement of 1 mg and the ability of the fecal organisms to manufacture the vitamin from intestinal contents result in the rare occurrence of a true avitaminosis If present it is rapidly relieved by substitution therapy (p 630)

Malabsorption —Interference with the absorption of vitamin K from the intestines is encountered in *ileitis colitis sprue* and other inflammatory conditions The exclusion of bile from the intestinal content also results in a deficient absorption of vitamin K in *obstructive jaundice* and with *biliary fistulas* The resultant hypoprothrombinemia with its tendency to ward bleeding is of great importance in projected operative procedures

The *treatment* of absorption deficiency requires the simultaneous oral administration of vitamin K and the bile salts or the parenteral administration of the vitamin alone

Insufficient Storage (Hemorrhagic Disease of the Newborn)—Insufficient storage of vitamin K gives rise to the clinical entity of Hemorrhagic Disease of the Newborn a syndrome which previously was regarded as a grave and often fatal disturbance The newer studies of vitamin K indicate that it is both preventable and curable

The prothrombin level of the newborn infant is about 80 per cent of

of a clot By their disintegration they supply thromboplastin whose quality must vary since thrombocytosis occasionally is associated with bleeding

Thrombocytes probably are manufactured in bone marrow from *megakaryocytes* They are apt to be deficient in medullary diseases such as *leukemia and aplastic and myelophthisic anemia* Under certain circumstances at least they are destroyed in the spleen so that certain types of *splenomegaly* (p 1129) are associated with thrombocytopenia In these *splenectomy* is followed by a marked thrombocytosis and alleviation of the hemorrhagic diathesis

Unknown Factors—Besides the recognized factors in the mechanism of blood coagulation there are other unknown factors which influence clotting This conclusion is justified by the fact that certain clinical conditions characterized by bleeding present normal laboratory findings For example the only abnormal test in hemophilia is the prolonged coagulation time In certain infectious diseases and profound renal insufficiency bleeding occurs in the presence of completely normal tests

Particularly with reference to the platelets qualitative changes seem to occur While bleeding is observed most commonly with thrombocytopenia it also may be present in certain instances of thrombocytosis Presumably the platelets are present in sufficient numbers but function with ineptitude

THE POSSIBLE SITES OF DIFFICULTY IN HEMORRHAGIC DISEASE

The survey of the agencies involved in the clotting mechanism suggests that hemorrhagic diatheses may follow disturbances in many diverse regions of the body These include the *circulating blood* the *bone marrow* the *liver cells* the *intestinal mucous membrane* and the *spleen*

The Circulating Blood—A tendency to bleeding accompanies the following disturbances of the circulating blood *hypoprothrombinemia* (p 1111) *thrombocytopenia* (p 1114) *thrombasthenia* (p 1117) *thrombocytosis* (p 1118) and *fibrinogenopenia* (p 1118) An additional factor may be responsible for *hemophilia* (p 1118)

The Liver Cell—Destruction or disturbance in the liver cell results in diminished or absent serum fibrinogen and hypoprothrombinemia either of which may contribute to a bleeding tendency These defects are observed in diffuse impairment of liver function as in *toxic hepatitis (p 1963) arsenical hepatitis (p 1964) and cirrhosis (p 1969)*

The Bone Marrow—Destruction replacement or relative absence of bone marrow produces a diminution in blood platelets (p 1114) However the blood platelets may be decreased when the bone marrow is normal or hyperplastic and they may be present in normal or increased numbers when the quality of clotting is impaired

The Intestinal Mucous Membrane—Disturbances of the intestinal mucous membrane prevent the absorption of vitamin K thereby producing a hypoprothrombinemia (p 1111) Exclusion of bile from the intestine prevents vitamin K absorption and leads to the bleeding tendency in jaundice These disturbances are remediable

The Spleen—In certain types of splenomegaly and probably in certain instances in which the spleen is not enlarged the increased destruction of the platelets results in a thrombocytopenia and splenectomy is followed by relief of symptoms

Clinical Manifestations of the Bleeding Diatheses—The theoretic possibilities in a bleeding diathesis have been discussed in the preceding paragraphs Practically not all of these circumstances are clinically evident So far as is known deficiencies of ionized calcium excess of antiprothrombin and thromboplastic deficiency do not occur

The undernoted classification lists the known clinical entities exhibiting bleeding diatheses

- Hypoprothrombinemia
  - Vitamin K Deficiency
    - Avitaminosis
    - Malabsorption
    - Insufficient Storage (Hemorrhagic Disease of the Newborn)
  - Prothrombin Deficiency

Disturbances of Blood Platelets
  Essential Thrombocytopenic Purpura
  Symptomatic Thrombocytopenia
  Chronic Hereditary Thrombasthenia
  Thrombocytosis
Fibrinogenopenia and Afibrinogenemia
Hemophilia
Disturbances of Capillary Permeability
  Hereditary Hemorrhagic Telangiectasia (Rendu-Osler Weber Disease)
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The prothrombin level of the newborn infant is about 80 per cent of

TABLE 76—DIFFERENTIAL DIAGNOSIS OF THE COMMONER BLEEDING DIATHESES

Variety	Sex	Age	Prothrombin Time	Platelets	Coagulation Time	Capillary Fragility	Specific Treatment
Hypoprothrombinemia (p 1111)	Both	Any age	Prolonged	Normal	Increased	Normal	Menadione (p 630)
Essential thrombocytopenia (p 1114)	More common in females	More common in middle age	Normal	Diminished	Normal	Increased	Splenectomy (p 1053)
Hemophilia (p 1118)	Male	Newborn to adult life	Normal	Normal	Increased	Normal	Transfusions Antihemophilic plasma fraction
Hereditary Hemorrhagic Telangiectasia (p 1119)	Both	Adults	Normal	Normal	Normal	Normal	Transfusions
Scurvy (p 1120)	Both	Children	Normal	Normal	Normal	Greatly increased	Cevitamic Acid (p 629)
Hemorrhagic Capillary Toxicosis (p 1121)	Both	Children	Normal	Normal	Normal	Normal	None

the adult figure It decreases normally in the first few days of life to approximately 60 per cent After the third day the content rises and reaches the adult level by the end of the first week of life In hemorrhagic disease of the newborn the rise is delayed and the fall is accentuated hemorrhagic phenomena appear when the level falls to approximately 20 to 30 per cent of the normal

Pathogenesis—In the era preceding the knowledge of vitamin K it had been observed that repeated small transfusions arrested the bleeding tendency and saved the life of the child although the mechanism of recovery was not clearly understood Studies of vitamin K reveal that the prothrombin deficiency of hemorrhagic disease of the newborn is probably related to disturbances in maternal metabolism as the result of which the infant is born without any store of prothrombin or vitamin K The child continues in a state of vitamin K deficiency for the first few days of life and the prothrombin level in the blood falls to a lower level with resultant hemorrhage Recovery follows the appearance of bile and bacteria in the intestinal tract with synthesis of the vitamin and satisfactory absorption

Clinical Manifestations—The clinical manifestations of the disturbance never make their appearance before the second day of life They may include continued bleeding from the stump of the cord hemorrhages into the skin or central nervous system bloody stools gross hematuria and bleeding from the mouth nose and ears eventually leading to death Delayed intracranial bleeding in the newborn also may result from the syndrome

Treatment

Hemorrhagic disease of the newborn is prevented by administering to the mother in the last weeks of pregnancy vitamin K or its precursor *Menadione* The active treatment of the infant is accomplished by the parenteral administration of 0.5 to 2 0 mg ($\frac{1}{130}$ to $\frac{1}{32}$ grain) of the vitamin or Menadione (p 630) Additionally a small transfusion of 20 to 50 cc of freshly drawn citrated blood is given since a delay of several hours follows the intravenous injections of water soluble preparations of vitamin K (p 630)

PROTHROMBIN DEFICIENCY

Hypoprothrombinemia that is not associated with vitamin K deficiency has a serious prognostic significance It occurs with severe diffuse liver disease and its presence is used as a functional test of the incapacity of that organ (p 1050)

Administration of vitamin K fails to alleviate this type of hypoprothrombinemia since prothrombin cannot be manufactured in the damaged organ Small amounts of prothrombin may be given by the transfusion of whole fresh blood but this cannot be kept up indefinitely Sooner or later if recovery of the hepatic cell cannot be accomplished the patient inevitably succumbs though not necessarily due to the bleeding Recent work indicates that fresh plasma or concentrated human beta globulin prepared by fractionation of plasma may be efficacious when administered parenterally in hypoprothrombinemia

Disturbances of the Blood Platelets (Thrombocytes)

Diminution in the number of circulating platelets is a probable cause of a bleeding tendency The condition of *thrombocytopenia* may be *primary* and idiopathic or *secondary* due to some more profound disturbance As a rare manifestation of a bleeding diathesis there may exist a *chronic hereditary thrombasthenia* In this condition the number of the platelets is normal but the function is apparently inadequate A similar situation apparently exists in certain instances of *thrombocytosis* associated with bleeding

Essential Thrombocytopenia (Thrombocytopenic Purpura Morbus Maculosus Werlhofi)

Essential thrombocytopenia is a specific bleeding diathesis that occurs at any time in life from early childhood to old age It is most often seen in middle aged females

Clinical Manifestations—*Essential thrombocytopenia may be acute and* rapidly fatal or chronic and recurring The latter may be severe eventually leading to death or mild with only partial inconvenience to the patient There is no hereditary aspect to the disease Although it is not present at birth the acute forms are most commonly seen in childhood Rarely the acute form in adults may be associated with marked toxicity jaundice and hemolytic phenomena progressing rapidly to a fatal issue Capillary thrombi are conspicuous the syndrome has been labeled acute febrile anemia with thrombocytopenia

Except for the rare occasions when the disease is encountered by chance in the performance of a routine blood count the presenting symptom of essential thrombocytopenia is *spontaneous bleeding* The initial bleeding may occur from any of the body tissues *Skin manifestations* which are rarely absent include showers of *petechiae ecchymoses* over the body and extremities and large subcutaneous *hematomas* These dermatoses *are not associated with any inflammatory reaction* The lesion is not surrounded by an erythema it is neither tender nor elevated it has no warmth and does not itch Besides the skin manifestations bleeding may be noted from the body orifices *nasal hemorrhages* may persist for days *uncontrolled by local hemostasis uterine bleeding may be manifest by* changes in the duration rhythm or severity of the menses or by inter menstrual bleeding

The disease is not accompanied by any arthritic manifestations the lymph nodes are not enlarged except as the result of secondary *infection* neither the spleen nor the liver is significantly enlarged nor unduly palpable Elevation of temperature does not occur except in fulminating forms as an association of an incidental infection or with internal bleeding

Laboratory Findings—The characteristic laboratory finding is a *thrombocytopenia* In the severer forms it may be impossible to identify any platelets whatsoever The usual count approximates 5000 and never exceeds 100 000 per cubic millimeter

There is not any necessary correlation between the platelet count and the degree of bleeding The hemorrhagic tendency is dependent not only upon the platelets but to a lesser degree upon the integrity of the capil

lary endothelium Thus while patients with platelets below 30 000 per cubic millimeter usually bleed some may not Others with counts approximating 100 000 may suffer from active hemorrhage The *bleeding time* is prolonged to fifteen or more minutes the *coagulation* time is usually normal or slightly prolonged clot retraction is poor and the clot is often soft and friable The tourniquet pinch and snake venom tests are usually positive

The other laboratory findings are dependent upon the degree of bleeding there may be a greater or lesser degree of *anemia* following any extensive hemorrhage signs of bone marrow activity are present in the peripheral blood there is usually a leukocytosis with a *shift to the left* and rarely a lymphocytosis

Diagnosis —The presence of any significant abnormality in the red or white cells points to the possible presence of a more fundamental blood dyscrasia with a *secondary thrombocytopenia* (p 1117) A diminution in the red cells beyond the results of hemorrhage suggests a profound disturbance of the bone marrow such as a *myelophthisic anemia* (p 1091) With a leukopenia or lymphocytosis there may be an *aplastic anemia* (p 1090) or an *aleukemic leukemia* (p 1105) The finding of abnormal immature leukocytes in the circulating blood gives rise to the suspicion of a *leukemia* (p 1100)

Under any circumstance the patient is referred to the specialist hematologist The bone marrow is examined by puncture which may have to be repeated several times before a definitive diagnosis is made By the examination of the bone marrow the expert may discover the presence of some more fundamental disturbance such as *multiple myeloma* (p 1126) a *leukemia* (p 1100) an *aplastic anemia* (p 572) *Gaucher's disease* (p 113") or a *metastatic carcinoma* (p 572)

The Course of the Disease —The course of idiopathic thrombocytopenia is unpredictable During a first attack the patient may progress rapidly to a fatal termination unaffected by any therapy At the other extreme mild instances are observed with complete subsidence in a few weeks or months this happy outcome is most often seen in children when the onset is in association with an infectious disease

Most often thrombocytopenic purpura progresses to a chronic recurrent hemorrhagic phase The blood platelet level never rises but the patient may lead a relatively normal life punctuated by exacerbations and remissions An accidental injury pregnancy or an emergency operation may result in uncontrollable bleeding

Treatment —The specific and curative treatment of idiopathic thrombocytopenia is *splenectomy* (p 1053) The decision to perform the operation requires consultation with an expert since there are many variables which require consideration

In the presence of brisk bleeding the patient is treated by repeated transfusions of fresh blood using the indirect method Though the bleeding tendency usually diminishes following transfusion the tendency to hemorrhage occasionally becomes more severe In the free intervals the patient is protected from trauma since shaving cutting of the finger nails brushing of the teeth straining at stool and blowing of the nose may institute bleeding Medication is given orally and hypodermics are avoided

Disturbances of the Blood Platelets (Thrombocytes)

Diminution in the number of circulating platelets is a probable cause of a bleeding tendency The condition of *thrombocytopenia* may be *primary* and idiopathic or *secondary* due to some more profound disturbance As a rare manifestation of a bleeding diathesis there may exist a *chronic hereditary thrombasthenia* In this condition, the number of the platelets is normal but the function is apparently inadequate A similar situation apparently exists in certain instances of *thrombocytosis* associated with bleeding

ESSENTIAL THROMBOCYTOPENIA (THROMBOCYTOPENIC PURPURA MORBUS MACULOSUS WERLHOFI)

Essential thrombocytopenia is a specific bleeding diathesis that occurs at any time in life from early childhood to old age It is most often seen in middle aged females

Clinical Manifestations—Essential thrombocytopenia may be acute and rapidly fatal or chronic and recurring The latter may be severe eventually leading to death or mild with only partial inconvenience to the patient There is no hereditary aspect to the disease Although it is not present at birth the acute forms are most commonly seen in childhood Rarely the acute form in adults may be associated with marked toxicity jaundice and hemolytic phenomena progressing rapidly to a fatal issue Capillary thrombi are conspicuous the syndrome has been labeled acute febrile anemia with thrombocytopenia

Except for the rare occasions when the disease is encountered by chance in the performance of a routine blood count the presenting symptom of essential thrombocytopenia is *spontaneous bleeding* The initial bleeding may occur from any of the body tissues *Skin manifestations* which are rarely absent include showers of *petechiae ecchymoses* over the body and extremities and large subcutaneous *hematomas* These dermatoses are not associated with any inflammatory reaction The lesion is not surrounded by an erythema it is neither tender nor elevated it has no warmth and does not itch Besides the skin manifestations bleeding may be noted from the body orifices *nasal hemorrhages* may persist for days uncontrolled by local hemostasis *uterine bleeding* may be manifest by changes in the duration rhythm or severity of the menses or by intermenstrual bleeding

The disease is not accompanied by any arthritic manifestations the lymph nodes are not enlarged except as the result of secondary infection neither the spleen nor the liver is significantly enlarged nor unduly palpable Elevation of temperature does not occur except in fulminating forms as an association of an incidental infection or with internal bleeding

Laboratory Findings—The characteristic laboratory finding is a *thrombocytopenia* In the severer forms it may be impossible to identify any platelets whatsoever The usual count approximates 5000 and never exceeds 100 000 per cubic millimeter

There is not any necessary correlation between the platelet count and the degree of bleeding The hemorrhagic tendency is dependent not only upon the platelets but to a lesser degree upon the integrity of the capil

the better in the hematologic picture yet the clinical result may be eminently satisfactory

SYMPTOMATIC THROMBOCYTOPENIA

Symptomatic thrombocytopenia occurs from a number of known or presumed causes and as an accompaniment of some more profound disturbance of the blood and blood forming organs

From Drugs and Chemicals —Idiosyncrasy to or poisoning by toxic chemicals may result in a thrombocytopenia Destruction of platelets has followed exposure to *arsenic gold ergot benzene sulfonamide* and *quinine* Under these circumstances it is important to recognize the causal relationship of the exposure to the drug Discontinuance of the agency may result in prompt relief whereas further exposure may produce a fatality

The symptomatic treatment of drug thrombocytopenia is identical with that of the essential type except that splenectomy is contraindicated

From Infection —Thrombocytopenia sufficiently severe to cause bleeding may be associated with many infectious diseases such as *typhoid fever meningococcemia subacute bacterial endocarditis* the *acute exanthemas tuberculosis* and *syphilis* Usually the platelet count rises when the infection is controlled Splenectomy is not recommended in the infectious types of thrombocytopenia

With Marrow Disease —Thrombocytopenia accompanies many of the profound blood disturbances such as *aplastic anemia leukemia metastatic carcinoma* of bone marrow *multiple myeloma Gaucher s disease* and *pernicious anemia* Under these circumstances the remaining hematological findings overshadow the thrombocytopenia Study of *marrow* obtained by sternal puncture may be necessary to establish the diagnosis

With Splenomegaly —The relationship between splenomegaly (p 1129) and thrombocytopenia is not entirely clear Under certain conditions the organ destroys an excessive number of platelets In the presence of splenomegaly with a bleeding tendency and thrombocytopenia improvement may follow splenectomy The decision concerning this procedure should be discussed with the expert *hematologist This relationship occurs most often* in Banti s syndrome (congestive splenomegaly) Gaucher s disease tuberculosis lymphoblastomas malaria Kala azar and schistosomiasis

CHRONIC HEREDITARY THROMBASTHENIA

Chronic hereditary thrombasthenia is a rare transmissible hemorrhagic tendency that occurs in males and females In the latter the disturbance is known as pseudohemophilia

The clinical manifestations are usually epistaxis and ecchymoses The platelet count clot retraction coagulation time and the tourniquet tests are usually normal but may yield varying results The bleeding time is usually prolonged These patients often stand surgical procedures without undue blood loss and the tendency to bleed recedes with advancing age

The course of chronic hereditary thrombasthenia is not affected by splenectomy Transfusion and supportive therapy are the only useful therapeutic agents

Specific Therapy—Various specific measures have been used and more or less abandoned The *oral administration of vitamins C K and P* has been advocated, *sodium citrate* has been given intravenously *parathyroid extract foreign protein epinephrine roentgen therapy to the spleen ultraviolet radiation* and *splenic artery ligations* have all been tried and abandoned The removal of a bleeding organ such as the uterus or kidney is dangerous and does not affect the course of the disease In all likelihood the occasional good result that was experienced from the use of any of the above efforts illustrated spontaneous cure rather than any specific therapeutic effect

Snake Venom—Injections of moccasin snake venom (p 1049) have been advocated but do not seem to affect the course in any predictable manner although they may hasten recovery in the acute forms of the disease The intracutaneous sensitivity is tested with 0 1 cc For therapy 0 1 to 1 cc of a 1 3000 dilution of snake venom is employed twice weekly in progressively increasing amounts Sometimes the reversal of a positive to a negative intracutaneous test as the result of subcutaneous therapy precedes clinical improvement

Splenectomy—When it has become obvious that the disease is not likely to terminate spontaneously in cure splenectomy is considered Ideally the operation is postponed until a partial remission when the bleeding tendency seems to be minimal and the hemoglobin and red cells have been restored to normal If the general condition of the patient is satisfactory the expectation of permanent cure is very high and the operative mortality is proportionately low Blood transfusions should precede and follow splenectomy At operation the surgeon is urged to seek and remove accessory splenic tissue There is a dramatic cessation of oozing as soon as the splenic artery and vein are ligated

In some instances the severity of the clinical picture and the relative lack of response to transfusion make splenectomy imperative despite unfavorable circumstances The operation is deferred in childhood if possible since youngsters have a greater chance for spontaneous cure The advisability of performing an interval splenectomy in individuals who are progressing favorably is debatable While it is true that a certain number of unnecessary procedures have been performed splenectomy has been deferred only to have the patient hemorrhage as the result of an insignificant trauma

Study of the *megakaryocytes* of the bone marrow provides an index of the probable result of splenectomy When the megakaryocytes are numerous the operation is indicated and a satisfactory result may be anticipated When the megakaryocytes are sparse the operation is postponed and other measures are thoroughly tried for the expectation of success following splenectomy, in such instances, is not great and the thrombocytopenia and bleeding tendency often remain unchanged after operation

In more than half of the patients who recover after splenectomy there is almost sudden stoppage of bleeding although slight oozing may continue for a few days The blood platelets rise in number to a striking degree within twenty four hours after the operation and they may reach a supernormal level in ten days after which they fall gradually to normal levels and remain at this point In certain instances there is little change for

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THROMBOCYTOSIS

The paradoxical combination of thrombocytosis abnormal bleeding and intravascular thrombosis is seen occasionally in chronic myeloid leukemia *polycythemia vera* so called essential thrombocytosis and after splenectomy It is assumed that an abnormality exists in the quality of the platelets

FIBRINOGENOPENIA AND AFIBRINOGENEMIA

Fibrinogenopenia is a rare condition that may occur without known cause but most *often is associated with severe diffuse disease of the liver* (p 1068) The disturbance presents no therapeutic possibility beyond efforts directed at the hepatic disorder

Afibrinogenemia is a rare congenital bleeding disorder

HEMOPHILIA

Hemophilia which occurs only in the *male* is a *chronic* hereditary tendency to bleed after *slight trauma* *Usually present from birth* the condition is transmitted through the female and cannot be passed on by healthy males of a hemophiliac family Occasionally a family history is *not obtainable but this is the* exception

Clinical Manifestations—The hemophiliac starts life with *persistent bleeding* from the *umbilical cord* or after circumcision from the *prepuce* Later hemorrhages are experienced at a variety of sites There are frequent episodes of *epistaxis* and gum and wound hemorrhages after tooth extractions *hematuria melena* subcutaneous or intramuscular *ecchymoses* follow slight trauma repeated *hemarthroses* are observed particularly of the knee joint *The latter may have the appearance of acute arthropathies* and are usually accompanied by moderate pyrexia With frequent joint involvement there may be loss of function ankylosis muscular contractures and a *chronic anemia Uncontrollable hemorrhages may follow minor* operative procedures such as circumcision If the patient survives to adolescence the tendency to bleed seems to become lessened

Laboratory Data—*The only* persistent *abnormality in the blood* examination is the *prolonged coagulation time* which may persist for four or more hours The bleeding time usually is normal but may be somewhat prolonged The other hematologic findings are *relative to blood loss* and consist of an anemia with polychromatophilia and reticulation The white and platelet counts clot retraction prothrombin levels and the capillary fragility tests are usually normal

Pathogenesis—The mechanism of the abnormality in hemophilia is not definitely known It is presumed that the cause of the disease resides in the great stability and lack of agglutinability of the blood platelets They do not liberate thromboplastin when blood is shed and normal coagulation does not occur There is also a suggestion that some plasma factor may be involved in the incoagulability of the blood *This hypothesis has practical significance* in the therapeutic use of the readily available plasma

Diagnosis—In older children the combination of the arthropathy and the ecchymoses suggests *rheumatic fever* with a purpura *In the latter condition* however there are usually polyarthropathies the coagulation time is normal and the sedimentation rate is increased

Treatment —Hemophilia is prevented by urging the females of an afflicted family to practice contraception If they insist upon impregnation the child is examined immediately after birth and the coagulation time is established If the test is prolonged operative procedures such as circumcision are omitted and a small transfusion of whole citrated blood is administered as a prophylactic endeavor

The known hemophiliac child must be protected from all injuries since there is no known agency by which the fundamental coagulative defect may be permanently corrected Immediately a bleeding episode is encountered a small *transfusion* of 100 cc is given Infusions of *plasma* are often equally efficacious The administration of *placental* and *ovarian extracts* has not been helpful Injections of the antihemophilic fraction of human plasma and local applications of fibrin foam oxidized gauze and thrombin may terminate bleeding promptly

Hemorrhage from an accessible site requires expert handling Excessive pressure in an attempt to accomplish hemostasis may give rise to an extensive hematoma At times bleeding is specifically controlled by applying tampons soaked in normal blood blood serum or snake venom of the Russell viper (p 1049) Concentrated thrombin preparations may be of value in local therapy Aspiration of a hemarthrosis has potentialities for both good and harm Relief from the tension accomplishes amelioration of pain and lessens the tendency to chronic joint changes but may also serve to perpetuate the bleeding

A form of therapy that requires expert supervision involves the desensitization of the patient to *foul or sheep blood serums* A transitory state of sensitivity arises in approximately one week and lasts for an indefinite but short period of time During the span of hypersensitivity an intravenous injection of the serum may lessen hemorrhage This procedure is not recommended

Disturbances of Capillary Permeability

Increased permeability of the capillaries may produce a bleeding tendency despite the presence of normal clotting mechanisms These vascular abnormalities result from morphologic metabolic and possibly allergic phenomena

HEREDITARY HEMORRHAGIC TELANGIECTASIA (RENDU OSLER WEBER DISEASE)

In hereditary hemorrhagic telangiectasia there is a chronic malformation of portions of the capillary bed The affliction occurs in males and females and while the exact mode of inheritance is not known the characteristic is a mendelian dominant

Clinical Manifestations —The diagnosis of hereditary hemorrhagic telangiectasia is established by the demonstration of markedly dilated and tortuous *capillaries* which are usually best seen on the nasal mucous membrane under the tongue on the volar surfaces of the hands and fingers and on the malar region of the face Similar lesions occur in the bronchi the urinary bladder and pelvis or in the intestinal tract The skin also reveals innumerable scarlet pea shaped or mulberry angiomas With visible capillary disorders it is fair to assume that internal lesions also are present

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ency to bleed and evidences of extravasated blood The sore gums provoke anorexia and dysphagia There is often an associated *subperiosteal hem atoma* found over the thigh or the tibia In infancy the bony lesion causes considerable pain and gives rise to a pseudoparalysis of the lower extremity

The scorbutic bleeding may occur from any mucous surface Addition ally *there are usually visible perifollicular skin hemorrhages and a peri* follicular keratosis

Laboratory Data.—The hematologic findings in scurvy are characterized by their normalcy If facilities are available for the determination of cevi tamic acid levels in urine and blood an exact diagnosis can be established The vitamin is not demonstrable in the blood stream Following the inges tion of 500 mg of cevitamic acid little or none appears in the urine testi fying to the tissue hunger for the specific products

Diagnosis—A presumptive diagnosis of scurvy is established by the demonstration of increased capillary fragility (p 3708) In infancy radio graphs reveal a ground glass appearance of the extremity bones subperi osteal elevation calcification in the subperiosteal hematomas and broad *ening of the epiphyseal lines*

Treatment—The prevention and cure of scurvy are accomplished with such specificity that the therapeutic results constitute a definitive test. *The use of foods which are rich in vitamin C such as orange lemon or* lime results in complete disappearance of the avitaminosis within a week. A similar result is accomplished by the oral or parenteral uses of *cevitamic acid* in crystalline form using 500 mg daily The body becomes saturated with vitamin C and large amounts then appear in the urine

Since vitamin C deficiency rarely occurs as an isolated avitaminosis it is wise to assume that there is an associated deficiency of other min erals and vitamins In consequence a high vitamin diet is advised with the supplementary administration of at least a quart of milk daily and multivitamin products

HEMORRHAGIC CAPILLARY TOXICOSIS (HENOCH SCHÖNLEIN S PURPURA ALLERGIC OR ANAPHYLACTOID PURPURA)

Hemorrhagic capillary toxicosis is a systemic disturbance character ized by *fever and widespread capillary damage leading to confluent hem* orrhagic disturbances

Clinical Manifestations.—Hemorrhagic capillary toxicosis occurs most often in children and young adults The onset is usually sudden with elevation of temperature and a variety of localizing manifestations such as abdominal pain bloody diarrhea arthropathies and visible dermatoses The latter which are characteristic consist of an initial urticarial eryth ematous macular or papular eruption which later takes on the hemor rhagic and exudative appearances of a warm raised and tender purpuric spot Lesions tend to be symmetrical and are most numerous on the lower extremities where they may appear in repeated crops Corresponding to the visible skin lesions are similar disturbances throughout all of the mu cous surfaces these account for the arthritic and digestive complaints

The Course of the Disease—The course of a hemorrhagic capillary tox icosis like its clinical manifestations is variable unpredictable and unin fluenced by treatment In infants and young children the attacks are

The capillary lesions do not assume clinical importance unless they are associated with mild or repeated *hemorrhages* The nasal mucous membrane is a frequent site of bleeding and large epistaxes are encountered The disturbance may manifest itself early in life or it may not be significant until the patient has entered the fourth decade At this time the presenting complaint may be bleeding from a visible demonstrable lesion The diagnosis is established by inference when telangiectases and angiomas appear in patients with otherwise inexplicable attacks of hemoptysis hematemesis melena or hematuria

Laboratory Data—The blood examinations in hereditary hemorrhagic telangiectasia are conspicuously normal The blood loss may be sufficient to cause an anemia but the tests of coagulation and capillary permeability are normal

Treatment—There is no specific control for hereditary hemorrhagic telangiectasia At best the practitioner is able to compensate for blood loss by *transfusion* and the administration of *hematinics* The patient is warned to avoid trauma particularly to the nasal septum

The local treatment of the capillary abnormality presents many difficulties Cauterization of the bleeding point is often followed by a reappearance of the telangiectasis With epistaxis the nasal cavity is packed with tampons soaked in adrenalin thromboplastin or Russell snake venom When the bleeding is deep seated and inaccessible an attempt is made to increase blood coagulability by transfusion or injections of snake venom using 1 to 3 cc of a 1 3000 solution twice weekly

SCURVY

Scurvy results from a deficiency of vitamin C In contrast to hereditary hemorrhagic telangiectasia scurvy is a functional disorder of an anatomically normal capillary bed

Etiology—Scurvy was the first of the vitamin deficiencies to be recognized and cured In the days of sailing vessels when men made long voyages on small boats it was not unusual to have members of the crew suffer from the characteristic syndrome The recognition of the deficiency and the use of lime juice to prevent and cure scurvy are credited to Captain Cook and it was his practice that led the British sailors to be labelled 'limies *Infantile scurvy (Barlow s disease)* another *manifestation of vitamin C deficiency* was formerly a clinical manifestation observed with great frequency as the result of prolonged bottle feeding without supplementation

In modern medicine the scurvy of sailors and infants has become so rare as to be a curiosity Nevertheless vitamin C deficiencies are observed *in chronic alcoholics* whose money is spent for liquor in *psychotics* on hunger strikes or rigid self imposed food limitation in patients with *peptic ulcer* who remain on milk diets for prolonged periods of time with obstructive diseases of the upper intestinal passages and widespread disorders of the intestinal absorbing structures especially those that are accompanied by hypermotility and diarrhea as in *sprue*

Clinical Manifestations—*Scurvy is usually* recognized by the appearance of the *gums* The attention of the patient is drawn to the lesion by pain and bleeding Examination of the gingival tissues reveals swelling a tend

The use of rutin a flavanol glucoside merits trial when petechial hemorrhages are demonstrable Tablets of 20 mg are given three or four times daily Untoward effects have not been noted

During convalescence *foci of infection* are eliminated A tonsillectomy *in our opinion* is particularly advisable Those children whose families are known to be allergic are entitled to investigation for sensitizations Those who believe the disease to be anaphylactic in origin suggest nonspecific desensitization with the tuberculins but we have no great faith in this procedure

Bleeding of Unknown Cause

Apart from the hemorrhagic diatheses of known origin and the clearly defined clinical syndromes previously described easy bruising and recurrent epistaxes are encountered without any apparent causation in middle aged women At times these bleedings are associated with *menorrhagia* or *metrorrhagia* The patient is otherwise in good health and there are no other consistent findings

The preponderance of these bleedings in females and the time relationship suggest that they are the result of the *menopausal syndrome* (p 2595) and treatment is directed at this mechanism

Intravascular Thrombosis

Intravascular thrombosis is the antithesis of the hemorrhagic state and may arise from diametrically opposed influences Thus the coagulative tendency is increased by *thrombocytosis* and increases in *fibrinogen* and blood *prothrombin* Extravascular and hemodynamic factors which favor blood clotting include inflammation involving the walls of the veins or lymphatics trauma to the vessel wall slowing of blood flow increased venous pressure and combinations of these disturbances

Clinical Manifestations —Peripheral venous thromboses occur in several varieties whose differentiation is important from the standpoint of therapy *Phlebothrombosis* an intravascular clotting without significant perivenous inflammation is the common type of postoperative thrombosis *Thrombophlebitis* with inflammation of the vein wall is observed in the puerperium and in association with infections and injuries of the leg In *suppurative thrombophlebitis* pyogenic bacteria are found in the wall and the lumen of the involved vein *Phlebitis migrans* is an uncommon form of venous inflammation in which segments of several vessels show transitory evidences of thrombophlebitis This disturbance is encountered in *thrombo angiitis obliterans* (p 1029) Finally *venous ectasia* involves varicose veins or arteriovenous aneurysms of the extremities

Phlebothrombosis —Phlebothrombosis usually is encountered in the vessels of calf and thigh It is seen most often after prolonged bed rest in the postoperative period and following infections such as pneumonia and typhoid fever The lack of venous inflammatory process results in relatively free movement of the clot and the danger of *pulmonary embolization* (p 2096)

The presence of phlebothrombosis is suspected from systemic and local symptoms Often there is a rise in temperature and pulse rate When no other explanation for this occurrence is obvious the legs are examined and tenderness may be demonstrable along the course of the involved

short and benign though recurrences are the rule *Only* on rare occasions does death or an acute renal insufficiency develop After the active stage of the disease has terminated an *orthostatic purpura* may be observed when the patient stands for any length of time Older patients often develop an *acute glomerulonephritis* of an exudative type (p 2373) with widespread vascular disturbances that may end disastrously

Laboratory Data —There is no specific laboratory test for hemorrhagic capillary toxicosis There may be a mild hypochromic anemia and a slight leukocytosis The capillary fragility tests are normal as are the investigations for blood coagulation

Differential Diagnosis —The widespread and variegated clinical manifestations *of hemorrhagic capillary toxicosis* provide a wide range for diagnostic error The wary practitioner is constantly on the alert for the recognition of the disturbance and in the presence of abdominal and arthritic disorders never omits examination of the extremities for the characteristic purpuric spots

The abdominal symptoms of the capillary toxicosis are easily mistaken for an acute surgical condition such as an *intussusception* (p 1876)



Fig 934 —Purpura rheumatica

or an *acute appendicitis* (p 1881) Most confusing is the circumstance when the specific serohemorrhagic effusion of the bowel wall actually produces an intestinal obstruction so that both conditions are present simultaneously *Nevertheless before advising an exploratory laparotomy* the practitioner carefully examines the body for purpuric spots and advises surgical intervention with great hesitancy when there is an associated purpura

The joint manifestations of capillary toxicosis closely simulate *rheumatic fever* In point of fact the name *purpura rheumatica* has been frequently applied *to the disease though there is little question that the* causative organism of rheumatic fever is not responsible for the vascular affliction

Treatment —There *is no specific treatment for hemorrhagic toxicosis* A high vitamin high calory diet is prescribed with forcing of fluids *Salicylates* (p 3832) are useful when there are joint pains or effusions but may add to the digestive discomforts *when the manifestations are intestinal*

Courtesy of Dr P H Manson Bahr London England

heparin The former can be given orally but its effect is not observed for from twenty four to seventy two hours The duration of anticoagulation is variable and a single dose may last for one to fourteen days The course of the treatment is necessarily followed by frequent observations of the prothrombin time (p 1050) Dicoumarol acts by lowering the prothrombin level of the blood An attempt is made to maintain the concentration between 60 and 40 per cent Below 30 per cent severe hemorrhages may occur and as the level cannot be predicted the administration of the drug is fraught with danger and may be followed by widespread hemorrhagic manifestations often serious and occasionally fatal

The use of heparin has been simplified by the introduction of a preparation that can be injected subcutaneously This product produces ir coagulability of the blood within an hour and the effect may be maintained for several days by a dose of 200 to 300 mg See p 1050

The present summary of anticoagulant effects requires a weighing of possible gains and probable ill effects Our personal choice is for subcutaneous heparin despite the discomfort of the local reaction We entertain great fear concerning dicoumarin and have avoided its use The intravenous injection of heparin is tedious time consuming and expensive

Paravertebral Block —A signal increase in the treatment of thrombophlebitis and phlebothrombosis has been accomplished by the introduction of *paravertebral nerve blocks* which yield amazing relief of edema and local pain The lumbar sympathetic ganglia are injected with procaine alcohol or both thus releasing the vasomotor tonus of the vessels of the involved limb

Surgery —The great danger of phlebothrombosis is that of embolization and most surgeons now favor *ligation of the involved vein* in order to prevent the dissemination of blood clot Usually the femoral vein and its branches are carefully isolated If they are obviously involved in the active intravascular thrombosis a glass tube is introduced into the lumen of the vessel and any clot is sucked out When a free flow of blood has been obtained the vein is ligated and divided Heparin is then injected subcutaneously to prevent thrombi from forming at the operative site. Heparinization is continued for at least three to five days following operation

Bilateral femoral vein interruption is a safe procedure even with patients who are seriously ill It is indicated when patients develop obvious evidences of phlebitis with or without embolization and in those who develop embolization with or without obvious manifestations of phlebitis. The procedure prevents massive fatal pulmonary embolization its late consequences are notable by their insignificance consisting at most of mild swelling and pain of either or both legs

vessel This manifestation is best elicited by dorsiflexion of the foot At times the patient complains of spontaneous pain increased by motion and corresponding in its localization to the area of tenderness Later, the skin overlying the involved vessel may become red and warm though this is more common in thrombophlebitis A slight edema may be observed over the pretibial region Measurements of the circumferences of the calves show an increase of the involved side, weight bearing greatly increases all the discomfort

At times the local signs are minimal and the first indication of the disturbance is a *pulmonary embolization* The patient develops chest pain cough and bloody expectoration associated with elevations of pulse rate and temperature Unless the possibility of phlebothrombosis is suspected, the condition is regarded as a postoperative pneumonia'

Thrombophlebitis—Thrombophlebitis is often associated with evidences of arterial spasm The leg is cold pale or cyanotic with a weakened or absent arterial pulse Occasionally the vessels of the opposite leg are simultaneously involved The relief of the reflex spasm *by blocking of the vasomotor nerves*, furnishes a basis for therapy

Thrombophlebitis as opposed to phlebothrombosis may be accompanied by lymphangitic streaks up the leg The clot is held in place by the inflammation of the vein wall and embolization is less likely to occur

Course—The course of phlebothrombosis and thrombophlebitis is subject to great variation Undoubtedly many of the disturbances pass without notice or with minimal signs Others are progressive and migratory and may persist for weeks or months At any time particularly in a phlebothrombosis, an embolization may occur with serious or fatal consequences This outcome is most often seen in middle aged women who are flabby and soft and is unusual in muscular males accustomed to manual labor It is a complication that occurs more often in private practice than in ward practice It seems to be particularly commonly associated with *hysterectomy* (p 2558)

Treatment—The *prevention* of phlebothrombosis is indicated by the lessons learned from the clinical observations Preceding internal surgery particularly hysterectomy the woman is advised to *exercise* her legs and build up her musculature she is encouraged to move toes ankles and legs as soon as she has recovered from anesthesia The patient nurse and medical attendant are instructed to insist upon leg exercises at each meal visit medication or use of the urinal or bed pan The prophylactic administration of the *anticoagulants (p 1045) has great promise using the subcutaneous deposits of* heparin or oral dicoumarol in 300 mg doses immediately following operation Early ambulation (p 4122) is imperative

Active therapy for the phlebothrombosis involves general measures, the specific use of the anticoagulants and surgery

There is general agreement that upon onset of symptoms the leg should be rested and elevated on several pillows More courageous physicians have advocated the application of an elastic bandage to compress the superficial veins and advise early motion The senior editor who has gone through the experience of postpneumonic phlebothrombosis and pulmonary embolizations shudders at the very thought of this advice

Anticoagulants—The available anticoagulants include *dicoumarol* and

heparin The former can be given orally but its effect is not observed for from twenty four to seventy two hours The duration of anticoagulation is variable and a single dose may last for one to fourteen days The course of the treatment is necessarily followed by frequent observations of the prothrombin time (p 1050) Dicoumarol acts by lowering the prothrombin level of the blood An attempt is made to maintain the concentration between 60 and 40 per cent Below 30 per cent severe hemorrhages may occur and as the level cannot be predicted the administration of the drug is fraught with danger and may be followed by widespread hemorrhagic manifestations often serious and occasionally fatal

The use of heparin has been simplified by the introduction of a preparation that can be injected subcutaneously This product produces in coagulability of the blood within an hour and the effect may be maintained for several days by a dose of 200 to 300 mg See p 1050

The present summary of anticoagulant effects requires a weighing of possible gains and probable ill effects Our personal choice is for subcutaneous heparin despite the discomfort of the local reaction We entertain great fear concerning dicoumarin and have avoided its use The intravenous injection of heparin is tedious time consuming and expensive

Paravertebral Block—A signal increase in the treatment of thrombophlebitis and phlebothrombosis has been accomplished by the introduction of *paravertebral nerve blocks* which yield amazing relief of edema and local pain The lumbar sympathetic ganglia are injected with procaine alcohol or both thus releasing the vasomotor tonus of the vessels of the involved limb

Surgery—The great danger of phlebothrombosis is that of embolization and most surgeons now favor *ligation of the involved vein* in order *to prevent the dissemination of blood clot Usually the femoral vein and* its branches are carefully isolated If they are obviously involved in the active intravascular thrombosis a glass tube is introduced into the lumen of the vessel and any clot is sucked out When a free flow of blood has been obtained the vein is ligated and divided Heparin is then injected subcutaneously to prevent thrombi from forming at the operative site. Heparinization is continued for at least three to five days following operation

Bilateral femoral vein interruption is a safe procedure even with patients who are seriously ill It is indicated when patients develop obvious evidences of phlebitis with or without embolization and in those who develop embolization with or without obvious manifestations of phlebitis. The procedure prevents massive fatal pulmonary embolization its late consequences are notable by their insignificance consisting at most of mild swelling and pain of either or both legs

CHAPTER 53

DISTURBANCES OF THE BONE MARROW

THE significance of the bone marrow in hematopoiesis has been described elsewhere (p 1043) In the adult red marrow is the principal source of origin of erythrocytes granulocytes and thrombocytes The newer knowledge of marrow activity as revealed by studies of spreads obtained by sternal puncture makes it clear that many of the disturbances classified as diseases of the blood are actually lesions of the marrow

Only multiple myeloma remains to be discussed in the present chapter

MULTIPLE MYELOMA (KAHLER S DISEASE)

Multiple myeloma is a *malignant tumor* of the bone marrow and rarely of other tissues It is seen in middle and advanced life and is much more frequently observed now than formerly because of the ready use of examinations of sternal bone marrow

Clinical Manifestations—Multiple myeloma starts in an insidious manner Most often the history is one of persistent progressive *bone pain* of mild or excruciating nature The discomfort is most often lumbar sacral or in the ribs It is aggravated by motion and is associated with local tenderness loss of weight weakness pallor and spontaneous fractures As a result of collapse of bony structure almost any kind of neurologic disturbance may occur *Soft tissue masses attached to bone may be observed* especially on the skull On other occasions the major clinical signs arise from bone marrow involvement leading to unexplained *anemia* or a *purpuric state* with *thrombocytopenia* Kidney damage is almost invariably present and the patient may show the picture of *chronic renal insufficiency* without azotemia or the signs of *uremia* without hypertension Not infrequently there are episodes of colicky *abdominal pain* with nausea and vomiting *These may be due to uremia or the irritative neurologic lesions*

Pathology—The remarkable variety of symptoms is readily explained by the details of the underlying pathology Large numbers of plasma erythroblastic myelocytic or reticulum myeloma *cells are found throughout the bone marrow of the body They* replace the normal tissue and give rise to abnormal blood pictures or they destroy bones and lead to multiple moth-eaten lesions of the skull ribs sternum vertebrae pelvis and bones of the extremities They may invade soft tissues in the process of *myelosarcomatosis* to produce extra-osseous *masses* that interfere with the function of the adjacent organs In rare instances masses composed of myeloma cells are present in lymph nodes and the internal organs

Laboratory Findings —The growth of myeloma cells is very often associated with marked disturbances in endogenous protein metabolism The principal effect of these aberrations is the appearance in the urine of *Bence Jones proteose* (p 3673) This phenomenon may be constant or sporadic Occasionally multiple myeloma progresses under careful observation without the appearance of this substance

As this proteose passes through the glomerular membrane and down the kidney tubules it tends to precipitate and thus causes blockage When this process is advanced it destroys the renal parenchyma and causes *renal insufficiency* (p 2275) Bence Jones proteose may rarely occur in other bone marrow diseases such as leukemia metastatic carcinomatosis multiple bone sarcomas or polycythemia

The abnormality in protein composition is reflected also in the unusually *high serum globulin* (p 3713) detected by the serum *formol gel reaction* As a result of the hyperglobulinemia there is marked *rouleaux formation* of the red blood cells producing difficulty in performing blood groupings The hyperglobulinemia is responsible also for the extremely *rapid sedimentation* of the erythrocytes interference in red blood cell counting and hemoglobin determinations and the occasional occurrence of *amyloidosis* (p 7) When blood serum which contains Bence Jones proteose is heated at 56 C for inactivation prior to performance of the Wassermann reaction it may jell and on other occasions anticomplimentary reactions are observed

The *serum calcium* is frequently elevated but the values for phosphorus and phosphatase are usually normal The urea is often elevated and the Takata Ara test may be positive The morphological appearance of the peripheral blood is variable and neither characteristic nor diagnostic An anemia is usually present but its severity varies The hemoglobin is usually diminished in proportion to the fall in red blood count so that the color index is usually 1 or slightly less Hyperchromic anemia with color indices above 1 is unusual Nucleated red blood cells are present from time to time but the white blood count is usually within normal limits Rarely plasma cells are observed in the peripheral blood in the so called plasma cell leukemia The blood platelets may be normal or considerably reduced When the latter occurs the hemorrhagic state is probable

Differential Diagnosis —The diagnosis *of multiple myeloma is dependent* upon the findings of the *Bence Jones proteose* in the urine and the discovery of plasma cell bone marrow Without these laboratory guides the clinical manifestations may simulate a wide variety of conditions such as hyperparathyroidism Ewing tumor metastatic *carcinomatosis osteitis deformans* chronic renal insufficiency glomerulonephritis amyloid contracted kidney pyelonephritis hydronephrosis polycystic kidneys aplastic anemia aleukemic leukemia pernicious anemia refractory anemia essential thrombocytopenic purpura osteo-arthritis or spondylitis

Prognosis —The prognosis of multiple myeloma is always hopeless Most patients die within nine months of the detection of the disease

Treatment —There is no effective therapy for multiple myeloma Injections of 150 mg of stilbamidine (p 132) daily alleviate pain and may arrest the progress of the disease Roentgen therapy chordotomy and narcotics may be tried for analgesia

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CHAPTER 54

DISEASES OF THE SPLEEN, RETICULO-ENDOTHELIAL SYSTEM AND LYMPH NODES

THE SPLEEN

In addition to changes due to disturbances in the physiology of the blood the spleen is subject to the same clinical derangements as other organs Congenital anomalies mechanical neoplastic inflammatory and vascular afflictions are encountered The last include Banti s syndrome more accurately described as a chronic congestive splenomegaly

Anomalies of the Spleen

Anomalies of the spleen assume clinical importance in the surgical treatment of *hemolytic jaundice* and essential thrombocytopenic purpura One or more *accessory splenic masses* occasionally are present Unless these are recognized and removed splenectomy is unsuccessful and the condition *continues to be operative Accessory spleens have been found in such* unexpected places as the stomach gallbladder testes groin and retroperitoneal tissues Other less important splenic anomalies include absence of the viscus and deviations in size and shape

Movable Spleen

A movable or floating spleen may be discovered in any part of the abdomen In generalized visceroptosis (p 3488) the mobility is particularly marked and there may be resultant *torsion of the pedicle* Under these circumstances violent *left upper quadrant pain* (p 1042) is present demanding immediate surgical interference Unless there is complete certainty that the organ has not been irreparably damaged a splenectomy is required

DIFFERENTIAL DIAGNOSIS OF

Splenomegaly

CAUSE	DIAGNOSTIC FEATURES
Diseases of the Blood and Blood Forming Organs	Hemogram and marrow smears differentiat infectious mononucleosis leukemia polycythemia vera, pernicious anemia thrombocytopenic purpura, erythroblastosis foetalis sickle and target-cell anemias, and primary splenic granulocytopenia Get marrow spread or biopsy for Hodgkin s disease (p 1138) Do fragility tests in hemolytic types of icterus (p 1060) Get lymph node biopsy in suspected lymphosarcoma and other associated lymphadenopathies (p 1136)
Hepatic Disturbances	With atrophic and hypertrophic cirrhoses (p 1969) With hemolytic and infectious types of icterus Obtain tests of liver function (p 1947) Note fragility of red cells (p 370b) Look for leptospira in blood and urine (p 360)
Infections	In infectious mononucleosis typhoid fever brucellosis miliary tuberculosis typhus and Rocky Mountain spotted fevers congenital syphilis malaria histoplasmosis schistosomiasis kala azar and subacute bacterial endocarditis Examine blood smears for plasmodia (p 516) Get blood cultures and Wassermann reactions (p 54) Do agglutination tests for typhoid and typhus (p. 59) and skin reactions for brucellosis and tuberculosis (p 59) Examine stools for ova (p 1893) and spleen puncture for Donovan bodies and leishmania
Local Disturbances	Movable spleen Splenic cyst, abscess or neoplasm (p 1132) Twist of pedicle (p 1128)
Metabolic Disturbances	In amyloidosis note hepatomegaly and response to congo red test (p 7) In rickets with bone deformities and hemochromatosis with glycosuria and iron pigment in skin In chronic congestive splenomegaly (p 1130) with hepatic cirrhosis and anemia (Banti s syndrome)
Reticulo-endothelioses	In Niemann Pick Letterer Siwe and Gaucher s diseases (p 1133) Note characteristic cells in bone marrow (p 1043)
Vascular Disturbances	With thrombosis of portal or splenic veins (p 1130) Following splenic infarction, particularly in subacute bacterial endocarditis (p 1021) Get hemogram and blood culture

RUPTURE OF THE SPLEEN

Traumatic rupture of a *normal spleen* is possible though the condition is more often encountered in the *splenomegaly* (p 1131) resulting from malaria typhoid fever or a blood dyscrasia

Rupture of the *spleen is suspected when the patient complains of agonizing pain* in the *left upper quadrant* Quite rapidly generalized distress is noted and the pain may be referred to the left scapular region With internal hemorrhage there is an increasing anemia and a marked leukocytosis Often the condition is accompanied by moderate to severe shock (p 928)

Treatment requires the intravenous introduction of plasma or whole blood As soon as the condition of the patient warrants a laparotomy is performed and the spleen is removed

VASCULAR DISTURBANCES

The rich vascularity of the spleen and its unique blood supply produce a variety of clinical manifestations Acute and chronic congestions occur as in other organs Splenic infarcts and disturbances due to thrombosis of the splenic vein are probably of greater frequency than is generally *recognized In addition portal congestion produces the syndrome of* splenic anemia which was first described by Banti

ACUTE CONGESTION

Acute congestion produces a splenic tumor as observed in many of the infectious diseases such as *typhoid fever* and *malaria*

CHRONIC CONGESTION

With chronic congestion of the spleen resulting from generalized backward failure there *is rarely a palpable enlargement of the organ* This is in contrast to portal congestion next to be described

Even in advanced cardiac failure splenomegaly is not noted unless there is a superimposed *bacterial endocarditis* (p 1021) with its frequent local infarctions

SPLENIC INFARCTS

Splenic infarcts occur more often than is generally recognized Most often the condition is an unexpected autopsy finding In retrospect the clinical history then reveals that the patient had complained of pain in the left upper quadrant associated with an increase in the temperature and pulse rate The vast majority of the infarcts heal without incident Most are sterile but under unusual circumstances a septic infarct produces a splenic *abscess* (p 1132)

THROMBOSIS OF THE SPLENIC VEIN

Thrombosis *of the splenic vein occasionally occurs as an isolated* phenomenon but more often it is associated with narrowing of the portal vein or a cavernomatous transformation of that structure The condition is suspected when the spleen becomes greatly congested and enlarged in association with pain and tenderness in the left upper quadrant Often the condition is accompanied by copious recurrent *gastric hemorrhages*

The diagnosis is rarely established If suspected a *laparotomy* is advisable since a splenectomy may be associated with some relief of symptoms

CHRONIC CONGESTIVE SPLENOMEGALY (BANTI S SYNDROME—SPLENIC ANEMIA)

Congestive splenomegaly is a syndrome of childhood or adult life and is characterized by marked enlargement of the spleen anemia leukopenia usually thrombocytopenia a tendency to gastro esophageal hemorrhages and cirrhosis of the liver

Clinical Manifestations —The disease usually starts insidiously with lassitude weakness and pallor or a sense of fullness in the left upper quadrant due to *splenic enlargement* The first symptom may be severe *gastro intestinal hemorrhage* The course is progressive and prolonged and may be punctuated at any time by hemorrhage from esophageal varices In the later stages enlargement of the liver jaundice cirrhosis of the liver and ascites are noted Cirrhosis may be present early in the disease Purpura may occur in patients with thrombocytopenia

Laboratory Findings —Banti s disease is characterized by a moderate *normochromic anemia* but later as a result of hemorrhage *hypochromic* appearances develop *Leukopenia* is a constant finding but the differential blood count may be normal The blood platelets may be normal high or low The last finding is frequent in children whereas the first is more often found in adults The bone marrow may show a normoblastic hyperplasia or may be normal In the thrombocytopenic type the megakaryocytes are normal They may be increased in the rarer thrombocythemic form

Treatment —When a hypochromic anemia supervenes as a result of repeated hemorrhage inorganic iron is prescribed orally as 1 to 2 gm (15 to 30 grains) of *ferrous sulfate* *Transfusions* are required at the time of hemorrhage or splenectomy

Splenectomy is the only therapy which holds any promise of cure and should be performed often with an *omentopexy* before the development of emaciation cachexia uncontrollable anemia gastric hemorrhages cirrhosis of the liver or ascites The results of the operation are definitely superior in patients with thrombocytopenia The mortality from splenectomy is not prohibitive but is higher than in hemolytic anemia The cause of the splenomegaly may be found at operation in thrombosis narrowing or sclerosis of the portal or splenic veins or cavernomatous transformation of these vessels Recurrence of gastric hemorrhage or progression of the cirrhosis of the liver may occur after splenectomy

In patients with normal or elevated platelet counts there is usually a marked increase in platelets after splenectomy portal mesenteric or other venous thromboses may occur at this time Anticoagulants such as *heparin* are administered in an attempt to prevent these complications

Roentgen therapy of the spleen is of limited value and the resultant dense adhesions interfere materially with subsequent splenectomy

THE SPLEEN IN THE INFECTIONS

Splenic enlargement occurs in many acute and chronic infectious diseases The acute splenic tumors such as are seen in *typhoid fever* have only diagnostic significance A persistent splenomegaly that is sometimes of clinical importance occurs in *syphilis* *tuberculosis* *malaria* and *kala azar* In *malaria* and *kala azar* the hemolytic function of the spleen liber

Rupture of the spleen is suspected when the patient complains of agonizing *pain* in the *left upper quadrant* Quite rapidly, generalized distress is noted and the pain may be referred to the left scapular region With internal hemorrhage there is an increasing anemia and a marked leukocytosis Often the condition is accompanied by moderate to severe shock (p 928)

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lipoid metabolism Present knowledge is limited to mere description since little is known concerning the origin of the syndromes or the methods by which they can be treated (Arch Int Med 77 198 Feb 1946)

Gaucher's Disease (Large Cell Splenomegaly)

Gaucher's disease is a rare and at times familial disorder occurring at any age It is thought to be due to a dysfunction of intracellular lipid metabolism in the reticular cells of the spleen liver lymph nodes and bone marrow

Clinical Manifestations —The disease occurs in an *acute form* in infancy and in a *chronic form* in other age groups The symptoms may start in childhood adolescence or adult life The onset may be gradual with an awareness due to fullness or dragging sensation of a mass in the left upper abdominal quadrant or with progressive weakness and lassitude due to anemia or ecchymosis and hemorrhages from one of the orifices due to thrombocytopenia On other occasions the onset may be sudden with severe localized pain in the bones of the extremities fever and all the signs of an acute infection simulating an osteomyelitis

Physical examination almost always reveals *brownish skin pigmentation* and considerable to enormous *enlargement of the spleen* The organ is firm and not tender Some enlargement of the *liver* is often present but the peripheral lymph nodes are rarely involved Wedge shaped *pinguecular* thickenings of brownish tissue are often seen on the sclera and are of diagnostic importance in young patients With osseous lesions an unusual expansion of the distal end of the femur or humerus may be noted The vertebrae may be involved by osteoporosis giving rise to bony collapse and spontaneous fractures may occur

Laboratory Findings —The hemogram shows a mild to moderate hypochromic anemia leukopenia and thrombocytopenia The low platelets are responsible for the frequent occurrence of mild to severe hemorrhages Abnormalities in the roentgen appearance of the bones are fairly constant due to the growth of Gaucher's cells within the marrow The cortex of the bone is thin but the medullary cavities of many of the bones are enlarged giving rise to Erlenmeyer or flask shape deformities The blood lipoids are normal See p 5

Diagnosis —The clinical triad of splenomegaly pingueculae and bone changes characterizes Gaucher's disease but identification of the specific Gaucher cells by sternal *marrow puncture* is necessary for absolute diagnosis Rarely will splenic puncture or lymph node biopsy be required At autopsy kerasin the cerebroside involved in the disease can be identified

Prognosis —The prognosis of Gaucher's disease depends to some extent upon the age at which the disease starts When it first appears in childhood the outlook is poor but adults may live for several decades in a fair state of health Death is often due to a secondary infection tuberculosis severe anemia or uncontrollable hemorrhage

Treatment —Except for splenectomy on definitive indication the treatment of Gaucher's disease is symptomatic requiring a balanced diet and transfusions for the anemia Removal of the spleen is considered for palliation when the organ is enormous with uncontrollable anemia severe

ates the parasites and produces a condition wherein the viscus acts as an infectious reservoir Under these circumstances *splenectomy* has been advised and the results have been satisfactory

Splenomegaly of the *Egyptian variety* occurs in *schistosomiasis* (p 537) The parasites are lodged in the radicles of the portal vein and give rise to a type of liver cirrhosis Thrombosis of the splenic vein is frequent and may require splenectomy if the organ becomes abscessed or ruptures.

Abscess of the Spleen—Abscess of the spleen is usually multiple and results from the effects of a septic infarct The lesion is not suspected unless a rupture of the viscus occurs Under these circumstances there are the manifestations of a *general peritonitis* (p 1923) In patients who have been carefully observed it may be possible to note that the previously observed splenic tumor has disappeared At operation splenectomy offers technical difficulties and it may be necessary to be content with mere splenotomy and drainage

The Spleen in the Metabolic Disorders

Splenic enlargement occurs in *amyloidosis* and the *reticulo endothelioses* (p 1133) The deposition of amyloid material in the spleen does not alter the general symptoms or management of this disturbance

The Spleen in the Blood Dyscrasias

The participation of the spleen in the blood dyscrasias has received previous attention The importance of the participation of the spleen is greatest in the hemolytic thrombocytopenic and granulopenic processes since under these circumstances splenectomy may be curative

See *Chronic Familial Hemolytic Jaundice* (p 1061) *Acute Hemolytic Jaundice* (p 1064) *Thrombocytopenic Purpura* (p 1114) *Splenic Granulopenia* (p 1100) *Felty s Syndrome* (p 2916) *Polycythemia Vera* (p. 1093), *Cooley s Anemia* (p 1071) *Sickle Cell Anemia* (p 1065)

Tumors of the Spleen

Tumors of the spleen are exceedingly rare Benign neoplasms such as fibromas lymphangiomas and hemangiomas are often encountered at autopsy but have little practical significance Primary malignancies may be of the nature of a reticulum cell sarcoma a lymphosarcoma an endothelioma or a secondary deposit from a cancer

The *diagnosis* of splenic malignancy is made only at laparotomy or autopsy Splenectomy can rarely be accomplished before the condition has reached the stage of inoperability

Cysts of the Spleen

Simple cysts of the spleen are occasionally encountered More often they are parasitic and result from invasion with the *echinococcus* (p 1983) Under any circumstance exploratory laparotomy is advisable and splenectomy is accomplished with varying degrees of technical difficulty

THE RETICULO ENDOTHELIAL SYSTEM

A variety of obscure diseases have been described in which there is a disturbance of the reticulo endothelial system together with alterations in

deep reflexes may be absent pigmentation of the mucous membranes or skin is observed and a generalized lymphadenopathy is frequently present

Laboratory Findings—The demonstration of the typical cell of the disease is accomplished by examining bone marrow obtained by sternal puncture by lymph node biopsy or splenic puncture Vacuolization of the leukocytes is observed and a slight degree of lipemia occurs in the late stage of the disease



Fig 236—X rays of pelvis and femurs of same case as Fig 235 The irregular bony defects due to lipid infiltrations are very numerous

Treatment—There is no therapy of value Some prolongation of life may be effected by careful nursing procedures *Gavage feeding is usually necessary*

Letterer Siwe s Disease

Letterer Siwe s disease a rare affliction of infancy is a *non lipoid reticulo endotheliosis* It is characterized by an acute onset and a progressively downhill course in which splenomegaly hepatomegaly generalized lymphadenopathy osseous involvement and hemorrhagic tendencies are frequent There is no form of useful therapy

Xanthomatosis

Xanthomatosis is a condition in which *cholesterol* or *cholesterol esters* accumulate in reticulo endothelial cells There are numerous localized and

Ho sfall and Sm th Quart Jour Med

thrombocytopenia or recurring hemorrhages The mortality of the operation is high but not prohibitive

NIEMANN PICK S DISEASE (LIPOID HISTIOCYTOSIS)

Niemann Pick's disease is a dysfunction of the intracellular lipid metabolism of the *phospholipids* (*sphingomyelin*) It is manifested in the reticular and histiocytic cells of all the organs of the body by a foamlike



Fig 235—A boy with Hand Schuller Christian syndrome Note the large number of cutaneous lesions some of which are hemorrhagic *

degeneration This rare disease occurs only in infancy more often in females than males It has a constitutional and familial background

Clinical Manifestations—The disease usually starts in the first year of life with gradual loss of appetite and of spontaneous movements At this time or even earlier enlargement of the abdomen is observed The progression of symptoms is fairly slow but death from secondary infection almost always occurs before the end of the second year of life Cachexia pigmentation of the skin refusal to swallow food apathy deafness and blindness make their appearance

The clinical findings are those of extreme cachexia There may be a cherry red spot in the macula of the eye as in *Tay Sachs disease* (*Amaurotic family idiocy*) The liver and spleen are considerably enlarged the

* Horsfall and Smith Quart Jour Med

Pediculosis	With posterior cervical lymphadenopathy if head is involved, and inguinal enlargement with infestation of body
Reticuloendotheloses	In Niemann Pick Letterer Siwe and Gaucher s diseases (p 1133) Get marrow smear or biopsy
Serum Sickness	With urticaria and fever following injection of therapeutic sera (p 548)

generalized varieties of this condition some associated with high levels of cholesterol in the blood serum and others with normal levels

Xanthomatous involvement of the *coronary arteries* may give rise to the clinical picture of *coronary thrombosis* (p 983) and is suspected if cutaneous xanthomas are present Xanthomatous *biliary cirrhosis* is a state of chronic jaundice due to xanthomas of the bile ducts

Hand Christian Schüller Syndrome —In the Hand Christian Schuller syndrome the cardinal manifestations are due to defects in the *membranous bones* of the skull in association with *exophthalmos* and *diabetes insipidus* The disease occurs most commonly but not exclusively in children Skin xanthomas may be present The defects in the skull are so varied as to have given rise to the term geographical map skull The specific histologic diagnosis is made by biopsy or sternal puncture There is no know therapeutic approach of any value

THE LYMPH NODES

While the lymph nodes are intimately concerned with the diseases of the blood and blood forming organs their principal clinical disturbances are relative to infectious and neoplastic diseases *Localized lymphadenitis* and *lymphangitis* occur with many topical infections and a *generalized lymphadenopathy* (p 1136) features many chronic systemic infections *Neoplastic involvement* of the lymph nodes is usually secondary and most often carcinomatous

The clinical disturbances of the lymph nodes which relate to the hematopoietic organs include *lymphatic leukemia infectious mononucleosis lymphosarcoma follicular lymphoblastoma* and *Hodgkin s disease* The present material is concerned with the last three as leukemia and infectious mononucleosis are el ewhere described

Lymphosarcoma and Follicular Lymphoblastoma

Lymphosarcoma and follicular lymphoblastoma are tumorlike diseases that involve lymphoid tissue in various parts of the body

Path logy—In lympl o arcoma, the structure of lymphadenoid tissue is erased by a ma ked prol feration of lymphocytes These may spread beyond the confines of the normal tissues to invade ne ghboring o gans The cl anges are most commonly se n in the supe ficial or deep lymph nodes or in the lympho d tissue of th gastro-intest nal tract A type d noted as *reticulum c ll sarcoma* is characterized by the proliferation of the reticulum cells of the lymphadeno d t ssues

Follicula lymphobla toma (giant follicular hyperplasia or follicular lymphoma) is characterized by the dev lopment of huge lymph foll cles in the lymph nodes

DIFFERENTIAL DIAGNOSIS OF

Generalized Lymphadenopathy

CAUSE	DIAGNOSTIC FEATURES
Blood Dyscrasias	Hyperchromic anemia lymphatic leukemia follicular lymphoblastoma, lymphosarcoma leukosarcoma and sickle-cell anemia (p 1065) Diagnosed by *hemogram or lymph node biopsy*
Carcinomatosis	May be generalized or localized to drainage area Supraclavicular node in gastric malignancy axillary enlargement in breast lesions and inguinal *adenopathy in prostatic cancer* Get biopsy *(p 575)*
Hodgkin s Disease	Infectious granuloma with generalized lymphadenopathy Enlargement may be first seen in hilar region Get biopsy and look for eosinophilia (p 1138)
Infections	
Brucellosis	Generalized *lymphadenopathy* with positive blood culture or skin test (p 314) May require biopsy (p 575)
Filariasis	Recurrent swelling usually inguinal with organisms demonstrable by puncture or in *blood stream* (p 50)
Granuloma Inguinale	Venereal infection with spreading ulceration (p 475) Identify H ducreyi in lesion (p 475)
Histoplasmosis	With splenomegaly fever and leukopenia Isolate yeast from blood, *sputum or marrow*
Infectious Mononucleosis	Frequent idiopathic infection *with characteristic* hemogram, positive heterophile reaction, and false positive Wassermann (p 337)
Lymphopathia Venereum	Venereal infection with positive Frei test (p 472)
Plague	Epidemic disease *with bubo usually in inguinal* region (p 321)
Rubella	Mild eruptive disease of the young with morbilliform or scarlatiniform eruption and particular enlargement of posterior cervical glands (p 417)
Syphilis	*Localized lymphadenopathy in primary stage usually inguinal Generalized lymphadenopathy in secondary stage Get* darkfield and Wassermann *test (p 331)*
Tuberculosis	Chronic lymphadenopathy often with secondary infection and suppuration May be cervical hilar or mesenteric Do tuberculin reaction and sedimentation time Get biopsy if possible
Tularemia	*Satellite lymphadenopathy in region of bite (p 323) Get history of handling wild rodents and blood culture*
Multiple Myeloma	Skeletal disturbances with Bence Jones proteose in urine (p 1126)

CONTINUED

are t n i t r l pathognomonic Finally there is a gr ter n aw tl ert
t e with areas of necros and hyaline degeneration

Clinical Manifestations—Hodgkin's disease is sometimes preceded or ac companied at its onset by infections around the teeth and in the tonsils The first suggestion of any abnormality consists of a *painless enlargement* of one or more of the groups of *superficial lymph nodes* The swelling may be unilateral at first but more often there is glandular enlargement of the opposite side The nodes are neither painful nor tender and the overlying skin appears normal The swelling increases slowly and inexorably for sev eral months The first constitutional symptom is often an intractable *pru*

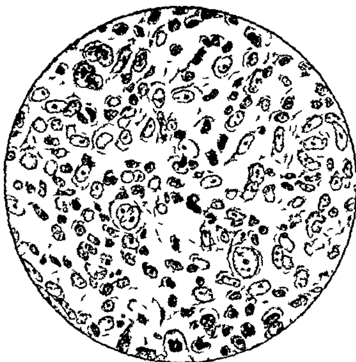


Fig 23 —Early stage of Hodgkin's disease Lymphoid and epithel i ll ll scatt i eosinophils and large multinuclear c ll

ritus Later other groups of nodes are noted to be involved in the supra clavicular axillary subpectoral mediastinal retroperitoneal mesenteric or inguinal areas The *spleen* is often palpable but rarely greatly enlarged The liver is usually palpable Infiltrations are noted in the pleura and lungs Areas of rarefaction are often visible in the radiographs of the long bones

Eventually the patient shows evidences suggesting a generalized cachexia The weight falls the blood pressure is low and pressure symp toms develop depending upon the ite of the lymphadenopathy Tracheal compression causes dyspnea dysphagia or paralysis of the recurrent laryn

Clinical Manifestations—The lymphatic neoplasms are most often seen in adult males and become manifest as localized swellings of the neck axillae or groins With involvement of systemic nodes the symptoms are those of pressure on various organs Enlargement in the nasopharynx with invasion of the base of the skull may give rise to cranial nerve paralyses tonsillar enlargements may occur, pressure on the trachea or bronchi produces distressing cough or hemoptysis involvement of the gastro intestinal tract may give rise to hemorrhage anorexia constipation or obstruction and invasion of bone and nerve tissue causes local pain In follicular lymphoblastoma the splenic enlargement results in discomfort in the left upper abdominal quadrant Fever sweating loss of weight and asthenia are commonly associated

Course—The lymph neoplasms pursue a fatal course within three to five years Follicular lymphoblastomas may become *leukemic* or acquire the characteristics of a *lymphosarcoma* Certain unusual instances of chronic lymphatic leukemia in which tissue changes of marked invasion are observed are regarded as 'leukosarcomas'

Diagnosis—The definitive diagnosis of the lymphatic neoplasm depends on histological study of excised tissue Except when associated with leukemia there are no specific blood findings The bone marrow in lymphosarcoma is not characteristic but infiltrations with lymphocytes or hematogones are observed in follicular lymphoblastoma

Treatment—Radiotherapy is effective for reduction in the size of masses and relief of pressure symptoms With lymphosarcoma of the stomach or other accessible parts of the gastro intestinal tract excision is worth attempting if there is minimal involvement of other tissues

HODGKIN S DISEASE

Hodgkin s disease is characterized by painless and progressive enlargement of the lymph nodes Often there is splenic enlargement and hypertrophy of the lymphoid tissue of other organs Later fever anemia and cachexia are encountered

Etiology—The cause of Hodgkin s disease is obscure As yet there is no clear conception of the pathologic classification of the affliction since many students believe that it is infectious and others regard it as neoplastic The infectious school recently attempted to include Hodgkin s disease in the syndrome of brucellosis but proof of the relationship is still far from satisfactory Other suggested infectious agents are the bacillus of avian tuberculosis and diphtheroids

Pathology—Hodgkin s disease is usually first observed in the cervical lymph nodes on either or both sides In the order of frequency the axillary inguinal mediastinal mesenteric and retroperitoneal glands are next involved The affected nodes are small when first noted but later they form large collections and chains with compression and displacement of soft parts and nerves Enlargement of the spleen occurs in more than half of the patients

Hodgkin s disease presents a characteristic histologic picture The lymphoid cells show evidence of hyperplasia with active proliferation in the germinal centers of the lymphoid follicles There is increased vascularity with proliferation of the reticulo-endothelium The lymph sinuses are dilated and partially filled with cells As the disease progresses the normal structure of the node is obliterated and a reticular network is observed in the meshes of which appear lymphocytes plasma cells many eosinophils epithelioid mononuclear and polynuclear giant cells The Dorothy Reed cell is a polynucleated giant cell and its appear

SECTION IX

THE ORGANS OF INTERNAL SECRETION

Associate Editor CLIFFORD R SPINGARN M D

geal nerves Edema occurs in an extremity effusions are noted in the chest or peritoneal cavity and there may be obstructive jaundice

Fever is a significant and very common accompaniment of the disturbance Most often there is a low grade and continued pyrexia The more sensational manifestation is the *Pel Ebstein* remittent type of fever with swings from normal to 104° or 106° F These violent fluctuations may be followed by an afebrile phase which lasts for days or weeks suggesting the temperature curve of a *brucellosis* (p 314)

Laboratory Data—There are no distinctive alterations in the blood In later stages a polymorphonuclear leukocytosis is encountered with a marked eosinophilia In abdominal forms a leukopenia may be encountered The laboratory diagnosis is dependent upon a biopsy of an accessible lymph node and the recognition of the characteristic pathology by the expert The *Gordon test* dependent upon the production of an encephalitis in rabbits injected with an emulsion of lymph nodes is credited with some specificity

Course—Though the clinical course of Hodgkin s disease is usually prolonged and marked sooner or later by the febrile changes previously noted (p 1140) other variations are encountered There is an *acute form* in which death occurs within a month A localized variation in the disease affects one group of lymph nodes for a considerable period of time though generalized extension is inevitably encountered The *mediastinal type* features pressure symptoms on the respiratory passages and a hypertrophic pulmonary osteoarthropathy The *abdominal forms* with jaundice diarrhea and ascites give rise to frequent confusion and a laparotomy often is performed unnecessarily except for the purpose of obtaining tissue for *microscopic study* *Some patients present a predominant splenomegaly* and others have most marked manifestations in the *periosteum* and *bone marrow*

Differential Diagnosis—The differential diagnosis of Hodgkin s disease involves a consideration of other causes for generalized lymphadenopathy such as tuberculosis lymphosarcoma follicular lymphoblastoma leukemia sarcoidosis syphilis infectious mononucleosis and metastatic carcinomatosis Attempts to clarify these problems on a purely clinical basis constitute a useless academic problem In place of idle speculation a *biopsy* is made and the definitive diagnosis is obtained from the pathologist

Treatment—The prognosis of untreated Hodgkin s disease is most unfavorable and the patient rarely survives beyond three years although with careful *roentgen therapy* patients have been reported to survive for fifteen to twenty years The exposure reduces the size of the tumor masses and often relieves pressure symptoms Forms of therapy which were previously used and have now been abandoned include excision of the glands tonsillectomy tooth extractions injections of bacterial vaccines made from glands in *Hodgkin s disease* and the various antiserums *Arsenic* may relieve the itching and is worth using in the intervals between roentgen therapy Pruritus is ameliorated by ergotamine tartrate (p 3883)

Experimental trials of nitrogen mustards using intravenous injections methyl-bis and tris-amine hydrochloride (0 1 mg per kg) appear to effect clinical remissions Therapy is not without risk and requires expert supervision

CHAPTER 55

INTRODUCTION METHODS OF DIAGNOSIS AND TREATMENT

ENDOCRINE or hormonal secretions are issued into circulating fluids by ductless glands and by organs which possess demonstrable excretory channels The latter include kidneys liver ovaries testes pancreas stomach and duodenum The more important ductless glands are the thyroids parathyroids anterior and posterior pituitaries and adrenal cortex and medulla

Vital and Nonvital Endocrine Structures—Certain of the hormonal structures are *essential* to life their destruction or surgical removal results fatally with specific or non specific symptoms The vitally essential endoctrine tissues are *pancreas parathyroids anterior pituitary* and *adrenal cortex* Other endocrine structures may be removed or destroyed without threat to the life of the individual but with the production of *specific deficiency manifestations* this situation prevails with reference to *ovaries testes posterior pituitary* and *thyroid* Finally a few of the ductless glandular organs seem *vestigial* and in experimental animals are removable without definitive threat to life or interference with normal economy these last include *thymus spleen* and *pineal body*

Experimental Endocrinology—Clinical endocrinology is clarified by the study of experimental ablation of endocrine structures and of injections of specific hormones In general the initial laboratory protocols consist of observations of animals from whom the endocrine structure has been removed in order to determine the nature of the deficiency syndrome The second portion of each experiment is the attempt to prevent or alleviate the deficiency syndrome by administration of the specific extract Finally the manifestations of overdosage are observed in the light of the symptoms of clinical hyperfunction Perhaps in no other branch of medicine is

syndromes the best proof of the correctness of any hypothesis is the improvement of the patient when the specific extract is administered in suspected hyperfunction alleviation of distress following diminution in or depression of glandular activity leaves little doubt as to the accuracy of the assumption

Hormone Assay —Except under experimental conditions it is not possible to do hormone assays in order to prove the existence of increased or decreased glandular secretion A notable exception is the pregnancy test in which the ovarian changes in the experimental animal are clearly due to an increased urinary excretion of gonadotropin

Metabolic and Other Laboratory Changes —On occasion indirect evidence of an endocrinopathy is obtained through the secondary changes that are produced in measurable laboratory tests elevation of the basal metabolic rate and an increase in blood iodine strongly suggest the presence of a hyperthyroidism a diminution in oxygen consumption leads to the suspicion that the patient is suffering from some form of lessened thyroidal activity Hyperglycemia occurs in diabetes mellitus hypoglycemia usually characterizes hyperinsulinism hypercalcemia is a constant finding in hyperparathyroidism with hypocalcemia appearing in parathyroid tetany blood cholesterol levels are elevated in diabetes mellitus and decreased in hyperthyroidism low figures for sodium and chloride with an increase in potassium values are observed in Addison s disease

Other laboratory phenomena may give information in the endocrine disorders vaginal cytology is an accurate index of the estrogen activity a characteristic hemogram is observed in macrocytic hyperchromic anemia destruction of the sella turcica is seen in expanding pituitary lesions a substernal shadow may be observed in the goitrous and adrenal cortical tumors produce distortions of the aerogram when a perirenal insufflation is made

METHODS OF TREATMENT

Non operative measures in the treatment of the endocrinopathies include substitution therapy stimulation and suppression of glandular activity irradiation and alterations in diet The surgical approaches are most often utilized in hypersecretory and neoplastic disturbances involving glandular structures

Substitution Therapy with Hormones —The hormones an important and clearly recognized group of endogenous drugs may be defined as discrete chemical substances secreted into the body fluids by certain cells for their specific effects on the activities of other cells The isolation of hormones suggests that the activities of the human organism are controlled and integrated by drug action the study of hormonal actions and effects constitutes the science of *autopharmacology*

The ductless glands on extraction yield both nonspecific and specific principles

Nonspecific Derivatives —Extraction of any living tissue reveals the presence of substances of demonstrable pharmacologic activity such as *histamine* a powerful depressant of smooth muscle which significantly lowers blood pressure The mere demonstration of a vasodilator effect from a tissue extract however need not necessarily have physiologic connotation It is misleading to conclude that the fall in blood pressure following the

and chloride metabolism the posterior pituitary substance is concerned with the disposition of water

Incidence of Endocrinopathies—Significant endocrinopathies are infrequently observed in clinical practice except for diabetes mellitus and thyroid disorders The rarity of ductless glandular disturbances is best emphasized by the actual records tabulated at the Johns Hopkins Hospital (Table 77)

The Twilight Zone of Endocrinology—A confusing and disturbing aspect of endocrinology has arisen through the unbridled claims of over enthusiastic specialists These scientists not content with demonstrable deficiency syndromes and definitive manifestations of hypersecretion see an endocrinopathy lurking behind every tree and have increased the scope of their subject to include formes frustes demonstrable in almost any human subject They have further embarked on endocrinologic analyses of personality manifestations sexuality criminology the arts and politics to the amazement of the ignorant and the chagrin of the informed

Most vulnerable claims seem to stem from a common error that is described by logicians as the fallacy of the undistributed middle Thus it is argued that

Patients with hyperthyroidism exhibit nervousness
Mrs Smith exhibits nervousness
Therefore Mrs Smith has hyperthyroidism

or

Castrates are shy timid and lack aggression
Mr Smith is shy timid and lacks aggression
Therefore Mr Smith is a castrate

It is a short step from this type of disordered logic to the supposedly indicated therapeutic program The alleged deficiency syndromes are treated by the administration usually by hypodermic of the indicated preparation the alleged manifestations due to hypersecretion are treated by injections of the supposed antagonists or the structure is exposed to roentgen rays with the idea of diminishing secretory activity At times the surgeons whet their scalpels and denervate or excise such structures as the adrenal medulla for the relief of hypertension (p 911)

It is small wonder under these circumstances that the practitioner entertains a degree of distrust for clinical endocrinology He has no way of knowing where science leaves off and damn foolishness begins The endocrinologists when confronted with these uncertainties ordinarily point to experimental investigations which are too complicated for interpretation or they retreat to the device of stating that the observation is based on clinical experience and proved through the medium of a successful therapeutic result The latter in most instances is accomplished by the force of suggestion the spontaneous evolution of the process or the *vis medicatrix naturae*

METHODS OF DIAGNOSIS IN ENDOCRINOPATHIES

The diagnosis of the endocrinopathies is essentially a clinical discipline with the therapeutic test as the most valuable adjuvant In the deficiency

TABLE 8.—THE RECOGNIZED ENDOCRINE SUBSTANCES

The products appearing in capital letters are described in the present chapter; those whose names are in normal type are elsewhere described and the reference is appended

Hormone	Origin	Principal Hormonal Action
POSTERIOR PITUITARY INJECTION U.S.P.	Posterior pituitary	Antidiuretic
GROWTH FACTOR	Anterior pituitary	Tissue and skeletal growth
GONADOTROPIC FACTOR	Anterior pituitary	Follicle and luteal stimulation
THYROTROPIC FACTOR	Anterior pituitary	Stimulation of thyroid
LACTOGENIC FACTOR	Anterior pituitary	Stimulation of mammary glands
CORTICOTROPIC FACTOR	Anterior pituitary	Stimulation of adrenal cortex
DIABETOGENIC FACTOR	Anterior pituitary	Insulin antagonist
KETOGENIC FACTOR	Anterior pituitary	Production of a [illegible] loss
THYROXIN U.S.P.	Thyroid	General metabolic stimulant
PARATHYROID INJECTION U.S.P.	Parathyroid	Regulation of calcium metabolism
INSULIN U.S.P.	Pancreatic insular tissue	Regulation of carbohydrate metabolism
Renin Renin Activator Angiotonin A[illegible]tonin Inhibitor	Kidney (p 22 3)	*Regulation of v[illegible]cular tension*
Prothrombin	Liver (p 1109)	P[illegible] blood co[illegible]ulation
Heparin	Liver (p 10 0)	Anticoagulant
Erythrocyte Maturation Factor	Liver (p 1033)	For erythropoiesis
Intrinsic Principle	Stomach (p 108)	For erythropoiesis
Secretin	Stomach (p 1935)	Stimulation of digestive ferments
Duodenin	Duod num (p 1 43)	Stimulation of digestive ferments
Villikinin	Small bowel (p 1821)	Regulation of motor activity
Enterocrinin	Small bowel (p 1821)	Regulation of digestive enzymes
Cholecystokinin	Gallbladder (p 1986)	Regulation of gallbladder activity
Enterogastrin	Stomach and intestine (p 1821)	Regulation of digestive enzymes
Estrogen	Ovaries (p 2515)	Regulation of ovulation and secondary sex characteristics
Progesterone	Corpus luteum (p 2517)	Regulation of ovulation
Gonadotropin	Placenta (p 2626)	Regulation of gonadal activity
Androgen	Testes (p 2401)	Regulation of spermatogenesis and accessory sex characteristics
EPINEPHRINE U.S.P.	Adrenal medulla	?
ADRENAL CORTICAL EXTRACT N.N.R.	Adrenal cortex	Regulation of sodium and chloride metabolism

injection of extracts of heart muscle and insulin free pancreatic tissue indicates that these structures possess specific internal secretory mechanisms for the control of vascular tension The practitioner must be alert to differentiate *pharmacologic* from *replacement responses* in the interpretation of tissue effects

Specific Hormones—The demonstration of a specific glandular product for any particular organ necessitates (1) evidence that the substance prevents the manifestations that result from clinical destruction or experimental ablation of the gland and (2) physiologic or chemical proof of the unique character of the product These requirements have been wholly or partially fulfilled for the agencies listed in Table 78

Chemical Composition—The hormones vary widely in chemical structure Thyroid anterior and posterior pituitary insulin and parathyroid hormones are proteins whereas adrenal cortical and sex hormones are steroids

The *protein hormones* must be obtained from animal tissues their chemical structure is not definitely known their use is often attended by diminishing responses to repeated injections (tachyphylaxis) and allergic reactions Of this group only the thyroid hormone is active after oral administration Being crude drugs these hormones must be assayed to insure uniform potency and they are usually dispensed in terms of biological units

The *steroid hormones* have been isolated chemically and are capable of synthesis In some instances synthetic preparations such as diethyl stilbestrol are superior to natural compounds These preparations or some modification are generally active after oral administration they do not require biological assay and dosage is expressed in terms of weight

Demonstrable Accomplishments of Substitution Therapy—The accomplishments of substitution therapy in the deficiency states include

1 Thyroid extract in *myxedema* (p 1193)
2 Insulin in *diabetes mellitus* (p 1246)
3 The anti anemic products in *macrocytic hyperchromic anemia* (p 1077)
4 Estrogen and androgen in female and male *hypogonadism* (p 2412)
5 Progesterone in *habitual abortion* (p 2519)
6 Gonadotropin in *hypogonadism* (p 2523)
7 Parathyroid extract in *tetany* (p 723)
8 Posterior pituitary extract in *diabetes insipidus* (p 1180)
9 Adrenal cortical substances in *Addison s disease* (p 1271)

Dangers of Substitution Therapy—Substitution therapy may be followed by untoward results often quite contrary to expectancy The ductless glandular products have widespread systemic influences When they are injected they may spray a number of structures other than the immediate target tachycardia and nervousness may result from thyroid extract administered for weight loss injections of androgen hopefully given for aphrodisiac effects often inhibit spermatogenesis and potency (p 2405) estrogen alleviates menopausal manifestations but may be carcinogenic the injection of protein hormones may lead to the production of anti hormones which nullify physiologic and pharmacologic endeavors

vitamin D are useful in tetany sodium chloride aids in the control of adrenal cortical deficiency

Surgery—The surgeon in concert with the internist and practitioner may point with considerable pride to the conquest of many disturbances due to hypersecretion in the internal glands His honor roll includes

Subtotal thyroidectomy in *hyperthyroidism* (p 1214) removal of *anterior pituitary tumors* (p 1175) parathyroidectomy in *hyperparathyroidism* (p 1225) partial pancreatectomy in *hyperinsulinism* (p 1242) splenectomy in hemolytic jaundice and other *blood dyscrasias* (p 1053) *removal of adrenal cortical tumors in virilism* (p 1271)

Artificial hormone therapy also is unsatisfactory in the sense that it is characterized by alternating periods of overdosage and underdosage in contrast to the normal economy in which hormones are liberated continuously in amounts which vary with physiological demands These difficulties are being overcome by the introduction of preparations such as protamine insulin that act slowly over a prolonged period

HORMONE RESISTANCE —The patient with a definite endocrine deficiency may fail to respond to specific hormonal substitution therapy due to a drug resistance This is seen in diabetes mellitus when enormous doses of *insulin may be required and in* the pituitrin resistant group of patients with diabetes insipidus In such cases the causes of refractoriness are unknown they may constitute the actual basis of the disorder by interference with the *normal activity of the endogenous hormones Refractoriness* differs from the acquired insensitivity that follows repeated injections of anterior pituitary and parathyroid preparations

HOMOLOGOUS GLAND ATROPHY —The use of endocrine products in poorly defined endocrine deficiency diseases or for their pharmacologic action in the absence of a specific glandular disorder is a threat to the functional integrity of the homologous gland The continued administration of desoxycorticosterone acetate to individuals with intact adrenal glands leads to adrenal cortical atrophy the use of thyroid for weight reduction may cause atrophy of the gland when the exogenous hormone suppresses the *formation of the hormone which occurs normally*

Stimulation —Until the recognition of the properties of anterior pituitary extracts the claims for stimulation of glands of internal secretion rested on a very dubious basis There can be no doubt currently however as to the ability of gonadotropic hormone to stimulate ovarian and testicular functions

Suppression —The anterior pituitary hormones are capable of repressing as well as stimulating the secretion of other organs of endocrine potential This property gives promise of future practical value although the present consideration is academic

A more concrete example of glandular suppression is available in the nature of *thio uracil* marketed as *Deracil* which gives definite evidence of a suppression of thyroid secretion in hyperthyroidism There is some *promise* that the successful introduction of this preparation may lead to a lessened necessity for performing the mutilating operation of subtotal thyroidectomy (p 1214)

Irradiation —Some of the normal and neoplastic ductless glandular tissues are radiosensitive roentgen therapy is of value in the production of artificial castration in male or female for shrinkage of benign and malignant tumors of the anterior pituitary glands and for control of the hyperplastic thymus *Many clinicians advocate roentgen therapy in hyperthyroidism* although our experiences with this method leave us in the ranks of the skeptics The efficacy of radioactive iodine is under current experimental test as another method for the control of hyperthyroidism

Diet —In endocrinologic disorders dietotherapy is chiefly used in the management of diabetes mellitus Iodine administration is of proven value in endemic goiter and the treatment of hyperthyroidism calcium and

numbers although there are extreme variations in normal differential counts The chromophobes are believed to be immature cells capable of differentiating into the other two types the acidophils elaborate growth hormone thyrotropic hormone and other associated principles the basophils are the probable source of gonadotropic hormone and function in the maintenance of adrenal cortical function

The *intermediate lobe* vestigial in man is separated from the posterior lobe by a cleft which is filled with colloid and irregular ves cles It consists of simple cords of pale staining cells which invade the pars nervosa Its function is unknown although it is believed to be the source of a melanophore principle

The *posterior lobe* consists of neuro-epithelial cells (pituicytes) wh ch contain secretory granules and a rich network of nerve fibers between which are interspersed pigment colloid inclusions cysts and free droplets The gland is connected with the hypothalamus by *supra optic hypophyseal* and *tuberohypophyseal* tracts whose nerve endings encircle the pitu cytes

The Anterior Pituitary Gland

PHYSIOLOGY AND PHARMACOLOGY

The physiologic importance of the anterior lobe hypophysis is best illustrated by a description of the effects of *anterior hypophysectomy* The results are uniform in all species of laboratory animals and may be consistently reproduced In young animals growth ceases sexual maturation is arrested and the other glands of internal secretion undergo involution in the adult appetite diminishes there is rapid weight loss reproductive activity ceases the capacity for mu cular work is reduced the basal metabolic rate falls increased sensitivity to insulin develops the glycogen reserve is depleted hypoglycemic episodes are encountered and resistance to infection is reduced The operated animal is unable to withstand various forms of environmental stress such as excessive heat cold or trauma and usually succumbs within a variable period

In contrast to the clarity of the effects of extirpation is the confusion attendant upon the results of injection of pituitary extracts Available preparations contain a mixture of a variety of principles some of which promote growth whereas others are gonadotropic thyrotropic corticotropic lactogenic diabetogenic or ketogenic Only the lactogenic principle has been isolated in pure crystalline form the remainder are proteins which are destroyed in the gastro-intestinal tract and which on parenteral injection lead to the production of anti hormones or antibodies The Council on Pharmacy of the American Medical Association has not yet placed the stamp of approval on any commercial preparation Nevertheless some have achieved popularity and are worthy of the consideration of the practitioner in deficiency syndromes and developmental anomalies

CLINICAL DISTURBANCES OF THE ANTERIOR PITUITARY GLAND

The complexity of the functions of the anterior pituitary gland is indicated in the paragraphs dealing with the physiology and pharmacology of the structure and is also attested by the variety of clinical disturbances which may become manifest in the human patient (Table 80)

Hypersecretion of the Acidophile Cells of the Anterior Pituitary Gland (Gigantism and Acromegaly)

Hyperactivity of the anterior pituitary acidophile cells in young individuals produces *gigantism* which is characterized by marked lengthen

CHAPTER 56

THE INTRACRANIAL GLANDS PITUITARY PINEAL

THE PITUITARY GLAND (HYPOPHYSIS)

THE pituitary gland is composed of morphologically and functionally unrelated portions The *anterior* pituitary gland is the master structure of the endocrine system studies of its functions and potentialities are still in their infancy The *posterior* lobe which yields potent pharmacologic substances seems of relatively slight physiologic and clinical significance

Anatomy—The human hypophysis is a small oval gland weighing from 0.5 to 0.6 gm in the male and 0.6 to 0.7 gm in the female It consists of a kidney shaped larger *anterior lobe* a smaller round *posterior lobe* which lies in the concavity of the anterior portion a rudimentary thin *intermediate lobe* between anterior and posterior lobes and the *pars tuberalis* a thin prolongation of the anterior lobe which invests the hypophyseal stalk

The gland lies within the *sella turcica* a depression in the sphenoid bone situated behind the sphenoid sinuses The sella is covered by a diaphragm of dura mater perforated by a small opening for the hypophyseal stalk The anterior superior portion of the gland is in relation to the posterior aspect of the optic chiasm which becomes compressed when the gland hypertrophies

The hypophysis is intimately connected with the *hypothalamus* by nerve fibers the most clearly defined of which link the supra-optic nucleus of the anterior hypothalamus and the posterior lobe (*supra optic hypophyseal tract*) Other neural connections exist between hypothalamus pars tuberalis and posterior lobe

The gland is abundantly supplied with blood from branches of the internal carotid arteries and the anterior and posterior communicating branches of the circle of Willis The venous outflow drains to the cavernous sinuses and the hypothalamus There is a capillary anastomosis between hypophysis and hypothalamus

Histology—The *anterior lobe* consists of irregular columns of epithelial cells separated by blood sinusoids Three distinct types of cells are differentiated the *chromophobe* variety is a small poorly staining cell with homogenous cytoplasm *acidophile* and *basophile* cells are large and granular and are adjacent to the blood sinusoids In the adult male chromophobes constitute 52 per cent, acidophils 37 per cent and basophils 11 per cent of the total

Etiology—The basis for acidophile cell hyperfunction in the anterior pituitary gland is usually an *adenoma* (p 1175) In certain cases of gigantism there is no distinct tumor but rather an increased number of acidophile cells The latter functional disturbances occur most often at puberty pregnancy or the menopause suggesting that the general endocrine upheaval at these times incites adenoma formation In gigantism there is probably an *additional hereditary factor* since familial examples have been observed in successive generations

Pathology—An adenoma produces gross enlargement of the pituitary gland As growth progresses the tumor erodes the sella turcica and stretches the tough dural membrane that extends between the clinoid processes The *optic chiasm optic tracts and hypothalamus* which lie above the tumor are often compressed but not to the same extent as by rapidly growing chromophobe adenomas In time the blood supply of the tumor becomes impaired and cystic degeneration occurs

TABLE 80—CLINICAL DISTURBANCES OF THE ANTERIOR PITUITARY GLAND

Physiologic Disturbance	Age of Patient	Clinical Syndrome
Acidophile Hyperfunction	Preadolescence	Gigantism
Acidophile Hyperfunction	Postadolescence	Acromegaly
Basophile Hyperfunction	Adult	Pituitary basophilism Cushing's disease
Anterior Pituitary Deficiency	Infancy	Pituitary dwarfism mongolian idiocy (?) Laurence-Moon-Biedl syndrome (?)
Anterior Pituitary Deficiency	Preadolescence	Fröhlich's syndrome adiposo-genital dystrophy
Anterior Pituitary Deficiency	Adult menopausal	Simmonds' disease adiposis dolorosa (?)

Incidence—Gigantism and acromegaly are rarely observed Gigantism occurs almost always in males acromegaly however is seen with equal frequency in females

Gigantism—In gigantism the skeletal changes that result from excessive growth stimulus are uniform and symmetrical As a result there is a marked lengthening of long bones due to increased formation of new bone at the epiphyses The tendency to gigantism has been observed in childhood but occurs more often at puberty In extreme instances heights of 8 to 9 feet have been observed

Normal and Eunuchoid Giants—Several types of gigantism are recognized The *normal* giant has upper and lower extremities of about equal length the span of the outstretched upper extremities approximates the height and the general appearance of the patient is that of a large but normally formed individual The *eunuchoid* giants possess shorter upper extremities and a span that is less than the height sooner or later if the patient survives there are superimposed deformities of acromegaly

ing of the skeleton The adult response to an identical endocrine stimulus is *acromegaly* marked by irregular and asymmetrical bony overgrowth
See *Differential Diagnosis of Increased Growth* (p 692)

TABLE 70—THE ANTERIOR PITUITARY HORMONES

Principle	Effect of Extirpation	Effect of Injection	Commercial Preparations (Unofficial)
Growth Hormone	Cessation of growth	Produces gigantism a positive nitrogen balance and stimulation of epiphyseal cartilage	Folvansin phykentrone (P) antuitrin growth phyon and growth complex
Follicle Stimulation (FSH)		In the female stimulates production of ova and granulosa cells and liberates estrogen in male stimulates spermatogenesis	Maturity Extracts Gonadotropic Factor Gonadophysin (P) and Prephysin (P) contain FSH and LH and are derived from anterior pituitary gland
Luteinizing Hormone (LH)		Stimulates thecal cells and favors production of progesterone in the female in the male stimulates interstitial cells and favors production of androgen	Anteron (P) Gonadin and Gonadogen (P) are equine gonadotropins obtained from the serum of pregnant mares
Gonadotropin	Atrophy of ovaries or testes	Combination of follicle stimulation and luteinizing hormones excretion in urine is basis of pregnancy test may be obtained from anterior pituitary glands pregnancy urine the serum of pregnant mares or placentas	Anterior pituitary like gonadotropic hormone anterior pituitary like sex hormone antuitrin-S A.P.L., chorionic gonadotropin follutein (P) korotrin (P) pranturon (P) and pregnyl (P) are chorionic gonadotropins obtained from the urine or the placentas of pregnancy
Thyrotropin	Thyroid atrophy and myxedema	Prevents thyroid atrophy after hypophysectomy	Unavailable continued injection leads to a refractory state probably due to the production of antihormones
Corticotropin	Atrophy of the adrenal cortex	Restoration of involuted glands to normal after hypophysectomy	Unavailable may produce antihormones
Lactogenic		Increased milk production in cows initiates lactation after parturition	Prolactin in doses of 200 to 300 international units may stimulate a delayed or deficient milk supply
Diabetogenic	Alleviates experimental diabetes	Produces experimental diabetes	Not obtainable
Ketogenic Principles		Increases catabolism of fat beyond the capacity of the body to oxidize ketone products	Not obtainable

Etiology—The basis for acidophile cell hyperfunction in the anterior pituitary gland is usually an *adenoma* (p 1175) In certain cases of gigantism there is no distinct tumor but rather an increased number of acidophile cells The latter functional disturbances occur most often at puberty pregnancy or the menopause suggesting that the *general endocrine upheaval at these times incites adenoma formation* In *gigantism* there is probably an additional hereditary factor since familial examples have been observed in successive generations

Pathology—An adenoma produces gross enlargement of the pituitary gland As growth progresses the tumor erodes the sella turcica and stretches the tough dural membrane that extends between the clinoid processes The optic chiasm optic tracts and hypothalamus which lie above the tumor are often compressed but not to the same extent as by rapidly growing chromophobe adenomas In time the blood supply of the tumor becomes impaired and cystic degeneration occurs

TABLE 80.—CLINICAL DISTURBANCES OF THE ANTERIOR PITUITARY GLAND

Physiologic Disturbance	Age of Patient	Clinical Syndrome
Acidophile Hyperfunction	Preadolescence	Gigantism
Acidophile Hyperfunction	Postadolescence	*Acromegaly*
Basophile Hyperfunction	Adult	Pituitary basophilism Cushing's disease
Anterior Pituitary Deficiency	Infancy	Pituitary dwarfism *mongolian* idiocy (?) Laurence-Moon-Biedl syndrome (?)
Anterior Pituitary Deficiency	Preadolescence	Fröhlich's syndrome adiposogenital dystrophy
Anterior Pituitary Deficiency	Adult menopausal	Simmonds' disease adiposis dolorosa (?)

Incidence—Gigantism and acromegaly are rarely observed Gigantism occurs almost always in males acromegaly however is seen with equal frequency in females

Gigantism—In gigantism the skeletal changes that result from excessive growth stimulus are uniform and symmetrical As a result there is a marked lengthening of long bones due to increased formation of new bone at the epiphyses The tendency to gigantism has been observed in childhood but occurs more often at puberty In extreme instances heights of 8 to 9 feet have been observed

Normal and Eunuchoid Giants—Several types of gigantism are recognized The *normal* giant has upper and lower extremities of about equal length the *span* of the outstretched upper extremities approximates the height and the general appearance of the patient is that of a large but normally formed individual The *eunuchoid* giants possess *shorter upper* extremities and a span that is less than the height sooner or later if the patient survives there are superimposed deformities of acromegaly

In contrast to the excessive growth of the skeleton the sex organs are atrophic and *impotence* is the rule The secondary sexual characteristics are undeveloped and despite the appearance of strength there is marked *muscle weakness* Most giants are mentally abnormal slow retarded and emotionally apathetic With hypothalamic involvement excessive obesity is added to the gigantism

Acromegaly—Acromegalic changes are noted when anterior pituitary hypersecretion occurs beyond the ages of about eighteen to twenty after



Fig 238—The Minneapolis giant 2184 mm (7 ft 0 in) beside Dr J S M 1763 mm (5 ft 9½ in net) *

the epiphyses have already closed The short and flat bones continue to grow and acral deformities are produced the mandible becomes especially prominent giving the appearance of prognathus hands and feet are en larged and phalanges are thickened arrow shaped mushrooming of the tips of the distal phalanges is observed and the terminal phalanges of the thumbs are hooked bony exostoses are frequent in many areas the bones of the calvarium thicken and the frontal sinus appears distended enlarge

* Gray H. Ann Int Med Vol 10

ment of the upper thoracic vertebrae produces a marked *kyphosis* exag gerated by the increased size of the scapulas

See *Differential Diagnosis of Increased Growth* (p 692)

Splanchnomacria—In addition to the skeletal overgrowth there is a splanchnomacria the *skin* connective tissues and mucous membranes become diffusely hyperplastic the *tongue* is large and protrudes from the oral cavity redundancy of the nasal mucous membrane and turbinates may produce complete occlusion of the nasal passages the *larynx* is ex tremely enlarged and the *vocal cords* are thickened and elongated hyper

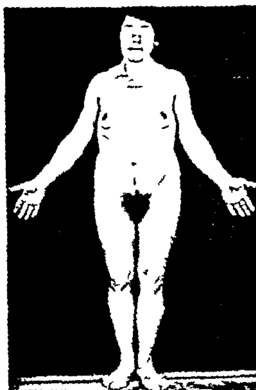


Fig 239—Acromegaly Single woman age 40 six years after onset of disease Amenor rhea alternating with menorrhagia Note large feet and hands with spadelike fingers and heterosexual distribution of pubic hair

trophy of the lungs heart gastro intestinal tract spleen and kidneys completes the picture Often there is a hyperplasia of the *adrenal cortex* enlargement of the persistent *thymus* and increase in pancreatic insular tissue the thyroid is often hyperplastic and a *colloid goiter* is present in almost a third of the patients In sharp contrast to the increased volume of the other endocrine glands the *gonads* are small or atrophic Adult acromegalics usually develop symptoms between the ages of thirty and forty The course of the affliction is slow and insidious and the fully de veloped clinical picture may take ten years to be completed

* Hoffman, Female Endocrinology

In contrast to the excessive growth of the skeleton the sex organs are atrophic and *impotence* is the rule The secondary sexual characteristics are undeveloped and despite the appearance of strength there is marked *muscle weakness* Most giants are mentally abnormal slow retarded and emotionally apathetic With hypothalamic involvement excessive obesity is added to the gigantism

Acromegaly —Acromegalic changes are noted when anterior pituitary hypersecretion occurs beyond the ages of about eighteen to twenty after



Fig 238 —The Minneapolis giant 2134 mm (7 ft 0 in) beside Dr J S M 1763 mm (5 ft 9¼ in net) *

the epiphyses have already closed The short and flat bones continue to grow and acral deformities are produced the mandible becomes especially prominent giving the appearance of prognathus hands and feet are en larged and phalanges are thickened arrow shaped mushrooming of the tips of the distal phalanges is observed and the terminal phalanges of the thumbs are hooked bony exostoses are frequent in many areas the bones of the calvarium thicken and the frontal sinus appears distended enlarge

* Gray H. Ann Int Med Vol 10

to maintain a profuse polyuria with nocturia *Dyspnea* on exertion and attacks of paroxysmal dyspnea may be encountered Peculiar mental changes are frequent and psychoses may be present

See *Differential Diagnosis of Gain in Weight* (p 695)

The *general appearance of the patient* is sufficiently characteristic to suggest the diagnosis of Cushing's syndrome The face has a full moon like appearance due to the deposition of fat around the cheek bones temples orbital regions and at the angles of the jaws the palpebral fissures are narrow and slitlike suggesting a *porcine facies*, the fat deposits are soft at first but soon become hard the overlying skin is thin tense and

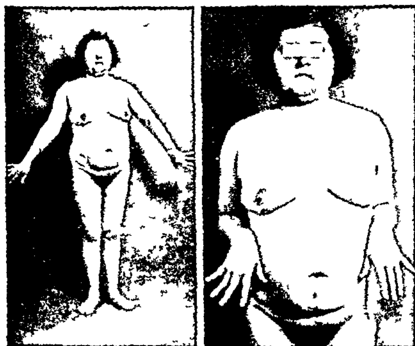


Fig 24?.—Cushing's syndrome Buffalo type of obesity facial hirsutism and purplish striae on lower abdomen Blood pressure 160/90 Very low sugar tolerance B.M.R -12 Sella turcica negative Exploratory operation revealed adrenal cortical hyperplasia without tumor formation Partial regression of facial hirsutism followed x ray radiation of pituitary and adrenal regions

has a florid bronze color uncomfortable drawing sensations in these areas may become sufficiently severe to prevent sleep

In females a dark heavy growth of *hair* occurs on the chin upper lip and cheeks but the scalp hair is thin There is an increased growth of hair on the chest around the areolas of the breasts on the abdomen and on the extremities The female pubic hair distribution takes on the characteristics of the male In males there is a tendency to lose scalp and body hair

The neck and trunk like the face are obese whereas the extremities

uniform clinicopathologic entity since a similar picture occurs in patients with tumors of the *adrenal cortex* the *thymus* and the *pineal* and with ovarian *arrhenoblastomas*

To avoid confusion it seems best to designate the symptom complex described by Cushing as Cushing s Syndrome' regardless of actual eti ology and to use the term pituitary basophilism' or Cushing's disease for those caused by a basophile adenoma of the anterior lobe

Etiology—While a *basophile adenoma* was present at postmortem in six of Cushing s eight cases the nosologic status of this neoplasm is not firmly established Basophile tumors have been encountered in the anterior lobe as incidental findings in routine autopsy material and the syndrome has been observed in the absence of this lesion In 1936 Crooke reported a peculiar hyalinization of the cytoplasm of the basophils in Cushing s syndrome He re garded this finding as the most constant anatomic feature of the syndrome and felt that it indicated the primary origin of the syndrome in the anterior hypophysis However the sig nificance of Crooke s change is open to question since similar findings have been en countered in patients without Cushing s syndrome Some students of the disease believe that *hyperfunction of the adrenal cortex* is primarily responsible and that the pituitary findings are secondary phenomena

Pathology—The *pituitary* in Cushing s disease is not appreciably increased in size and the basophile adenoma may be so small as to be detectable only by study of serial sections The neoplasm though small is usually well demarcated and compresses surround ing pituitary tissue There is no mechanical compression of neighboring neural structures as in the case of chromophobe and acidophile tumors of the anterior lobe A peculiar hyalini zation and vacuolization of the cytoplasm usually occurs in the basophile cells of the an terior lobe but not in the basophile tumor itself

The *thyroid* may be slightly enlarged but is usually normal *parathyroids* are normal or fibrotic and infiltrated with fat there is little pathological evidence of parathyroid hyper function although parathyroid adenomas have been found the *pancreas* shows no signifi cant changes the *adrenals* frequently are hyperplastic their cortices are widened and well defined adenomas are often present the *ovaries* and *testes* are small and atrophic

The *heart* is usually hypertrophied and the larger *arteries* show varying degrees of atherosclerosis A moderate degree of nephrosclerosis is frequent The *bones* are soft, par ticularly those of the spine and thoracic cage which may be cut easily with a knife microscopic study reveals a marked thinning to the point of complete disappearance of the bony trabeculae the compact bone is thinned the bone marrow may show some erythro poietic hyperplasia but not sufficient to account for the osteoporosis

Incidence—Pituitary basophilism is rare a few instances have been observed in children but most examples occur in late adolescence and early adult life There is a definite predilection for the female

Pathogenesis—A fundamental question in pituitary basophilism and in Cushing s syndrome is the significance of the adrenal cortical participa tion To the best of present knowledge the pituitary lesion is primary due to the hypersecretion of adrenotropic factor by the basophile cells there is a secondary adrenal cortical hyperactivity In females this causes an increased output of androgens leading to masculinization and in males an excessive production of estrogens leading to feminization

Clinical Manifestations—The onset of pituitary basophilism is usually insidious The earliest complaints are *weakness increasing weight impo tence* in the male and *amenorrhea* in the female As the disease develops the patient suffers marked *asthenia* to the point of invalidism *Multiple aches and pains* are noted with particular severity in the lumbar regions *headaches* are frequent and may be attended by *dimness of vision* Many patients experience a moderate increase in *thirst* and drink sufficient fluid

nitrogen balance even on a fairly high protein intake According to Albright the essential metabolic defect is the excessive conversion of protein into glucose as a result of hyperfunction of the adrenal cortex This leads to a depletion of body stores of protein and is responsible for the weakness osteoporosis capillary fragility and the atrophy of the skin as well as the hyperglycemia and glycosuria

Roentgenographic Findings—The sella turcica is usually of normal size and shape but the outlines are often faint and indistinct because of the generalized osteoporosis The latter is most apparent in the cranial vault the spine may show a severe kyphosis the vertebral bodies are thinned

TABLE 81—DIFFERENTIAL DIAGNOSIS OF CUSHING'S SYNDROME

	Basophile Adenoma	Adrenal Cortical Adenoma	Arrhenoblastoma
Obesity	Face and trunk	Face and trunk	Not characteristic
Purple striae	Usual	Usual	Rare
Ecchymoses	Common	Common	Absent
Rubicundity	Usual	Usual	Absent
Acne	Common	Common	Not characteristic
Hypertension	Present	Present	Absent
Hirsutism	Present	Present	Present
Metabolic Changes			
Impaired glucose tolerance	Common	Common	Absent
Osteoporosis	Common	Common	Absent
Sexual Function			
Male			
Libido	Normal or diminished	Normal or increased	
Sexual development	Retarded	Precocious	
Female			
Libido	Normal or reduced	Normal or reduced	Normal or reduced
Menstruation	Abolished	Abolished	Abolished
Genitalia	Atrophic	Hypertrophy of clitoris	Hypertrophy of clitoris
Sexual development	Retarded	Precocious	Precocious

After Dorfman Wilson Peters

and may be greatly compressed Intravenous pyelograms and perirenal *aerograms are made in a search for indications of an adrenal mass*

Course and Prognosis—The course of the disease is progressive and the prognosis is poor unless adequate therapy is instituted The average duration of life without treatment is from three to five years The susceptibility of these patients to infections is definitely increased and death results from multiple cutaneous abscesses intercurrent erysipelas acute pulmonary complications or meningitis Operative procedures are poorly tolerated and have a high mortality

Differential Diagnosis—The clinical differentiation of *pituitary basophilism* from the other causes of *Cushing's syndrome* is difficult There are no really distinctive clinical features upon which a separation can in most

are thin and spindle like The trunkal obesity is often more apparent than real and is accentuated by the dorsal kyphosis and the lax abdominal musculature which allows the abdomen to protrude Despite the obese appearance of the face and trunk the total body weight may remain unchanged Many patients gain a moderate amount of weight as the disease develops but lose it during the subsequent course There is usually a well developed dorsal kyphosis which produces a distinct *loss in height* The thoracic curve is accentuated by a cervicodorsal fat pad The concentration of fat about the face neck shoulders and trunk has been termed the *buffalo type* of obesity

The skin especially of the face and chest has a dusky cyanotic hue suggestive of plethora many *telangiectases* are present and *acne* of the face and back is common wide purplish *striae atrophicae* produced by rapid stretching of the skin radiate from the groins over the abdominal wall and are present over the medial aspects of the thighs these vary in color from a deep to pale purple depending on their time of appearance and crops of *petechiae* and *ecchymoses* recur with frequency Further evidence of increased capillary fragility is indicated by a positive tourniquet test The skin of the anterior tibial surface often shows deep brown discoloration due to old ecchymoses The thin extremities are often edematous and show a distal or acral cyanosis The muscles are weak flabby and seem wasted Fractures are common and result from slight injury

The *blood pressure* may reach levels seen in the accelerated or malignant phase of essential hypertension the heart may be enlarged and overactive fundus examination reveals narrowing of the retinal arteries and retinal hemorrhages optic neuritis or papilledema

In both sexes the external genitalia are small and atrophic The uterus is small and infantile

Laboratory Data—The *hemoglobin* and *red blood counts* are usually normal or elevated This may be correlated with the occasional erythroid hyperplasia of the marrow The polymorphonuclear *leukocytes* are usually moderately increased to 15 000 or 20 000 per cubic millimeter

The *blood sugar* is abnormally high glucose tolerance is impaired and glycosuria is frequent The diabetic state is usually mild but if severe is difficult to control with insulin As in the cases of diabetes mellitus the *blood cholesterol* and *total lipid* contents are moderately increased

Despite the frequency of osteoporosis *calcium inorganic phosphorus* and *phosphatase* levels of the serum are not appreciably altered Hypercalcemia has been observed but in most instances the serum level is normal or subnormal Interesting changes in other serum electrolytes have been noted There may be sufficient increase in *serum sodium* and *bicarbonate* to produce alkalosis and tetany Under these circumstances serum *potassium* and *chloride* values are reduced

Mild *albuminuria* and microscopic *hematuria* are frequent findings in patients with well marked hypertensive disease Moderate limitation of renal concentrating power is common *Polyuria* and *polydipsia* have been observed without reference to the mild glycosuria These symptoms are uninfluenced by injections of pituitrin and are examples of pituitrin resistant diabetes insipidus

Studies of the intermediary metabolism of foodstuffs reveal a *negative*

tious processes The site of the primary disturbances may be in the hypothalamus or its neural connections

Clinical Manifestations—The first evidences of pituitary dwarfism usually become apparent during the latter half of the first decade the *failure of growth* and the delay in *sexual maturity* are accentuated with the onset of puberty In patients with intracranial lesions the disorder of growth is overshadowed by the symptoms and signs of *increasing intracranial pressure* these include headache vomiting impaired visual acuity optic atrophy papilledema ocular palsies bitemporal hemianopsia enuresis epileptic attacks hypersomnolence and hyperirritability

The *general appearance* is one of retarded growth and development The body is small but well proportioned the scalp hair is delicate and sparse the face is small and the features are poorly defined there is a wizened expression giving an appearance of old age (*facies progenica*) the skin is wrinkled thin and atrophic with numerous pigmented spots dentition is retarded and the teeth are small the voice is high pitched and childlike the genitalia are atrophic and underdeveloped there is no libido and females fail to menstruate These findings contrast sharply with the primordial proportionate dwarf (pigmy) whose sexual organs and functions are normal

Intelligence is usually normal dwarfs of this type are quite successful as entertainers In the presence of hypothalamic injury the dwarf may be obese and present the picture of *Frohlich s syndrome* This type is apt to be more sluggish and apathetic than the pituitary dwarf

See *Differential Diagnosis of Decreased Growth* (p 693)

Laboratory Data—The pituitary dwarf usually has a mild *anemia achlorhydria*, lowered *basal metabolic rate* increased *sugar tolerance* hypoglycemia and a flattened glucose tolerance curve The *urine* in the presence of diabetes insipidus is of large volume and low specific gravity

Roentgenograms reveal a small skull, the facial bones and nasal sinuses are underdeveloped the sella turcica may appear normal rudimentary small or completely bridged With a craniopharyngioma there is usually some suprasellar calcification and erosion of the clinoid processes Carpal and metacarpal development is normal unless there is a complicating hypothyroidism The bone centers of ossification are small and show poor massing The long bones are thin and fragile with a tendency to pointing of the distal phalanges The epiphyses remain open into adult life

Treatment—Replacement therapy with *growth hormone* and *androgen* has been successfully reported and is distinctly worthy of trial *Surgical intervention* is warranted if there is a suggestion of an expanding cyst or neoplasm Attempts at extirpation carry a high mortality since postoperative vasomotor collapse is common and nuclear hyperthermia may cause the rectal temperature to rise to 108–109° F *Irradiation* is of little value because of the resistant quality of the tissue

Mongolian Idiocy

Mongolian idiocy is a condition of unknown etiology whose prognosis is presently hopeless It is here classified with anterior pituitary disorders for want of more accurate information

Clinical Manifestations—The Mongolian idiot has oblique eyes and a

cases be made The diagnosis of *basophilism* is justifiable only after the other possible causes of the syndrome have been excluded and the re sponse to pituitary irradiation has been observed

Adrenal cortical tumors are excluded principally by roentgenographic studies of the kidney regions for evidence of a mass roentgenographic evidence of *metastases* indicates an adrenal cortical carcinoma Hyper trophy of the clitoris is in favor of an adrenal cortical tumor since the external genitalia are small and atrophic in basophilism Patients with adrenal cortical tumors may have high urinary values for androgen or 17 ketosteroids whereas in Cushing s syndrome without an adrenal tumor low values are found Another possible means of differentiation is the tremendous increase in the urinary excretion of *estrogen* with no increase in anterior pituitary like factor in patients with adrenal cortical carcinoma

An *arrhenoblastoma* may produce a clinical appearance which is highly suggestive of Cushing s syndrome The ovarian tumor is usually demon strable on bimanual pelvic examination and obesity hypertension hyper glycemia and osteoporosis are not usually present

Cushing s syndrome due to a *thymic tumor* is rare and its presence is usually indicated by physical and roentgenographic evidences of a medi astinal tumor *Pineal tumors* are usually detectable roentgenographically

Treatment—If the diagnosis of pituitary basophilism is established with reasonable certainty an expert opinion is sought before treatment is instituted Roentgen irradiation of the pituitary region often produces some degree of improvement However the benefit is usually temporary and the results are totally unpredictable *Surgery* is not indicated because of the small size of the tumor *Radium implantation* after surgical ex posure has been tried but is technically difficult *Surgical exploration of the adrenals,* in two stages has been advocated to demonstrate an adrenal cortical tumor not visualized by x rays In the presence of suggestive hyper trophy even if an adenoma is not found *resection* of adrenal cortical tis sue is of some benefit Large doses of *estrogen* and *androgen* have been used with subjective improvement and a decrease in nitrogen excretion

Because of the negative nitrogen balance patients are given *high pro tein diets* (p 674) containing as much as 400 gm daily In view of the thirst polyuria high serum sodium and low potassium a *low sodium high potassium diet* (p 682) is worthy of trial Considerable improvement has been noted in patients to whom 15 gm of *potassium chloride* and *potassium citrate* were given daily

Anterior Pituitary Deficiency in Infancy and Childhood (Pituitary Dwarfism)

Insufficiency of the anterior pituitary gland during the period of most rapid somatic growth and development results in a form of dwarfism char acterized by a diminutive well proportioned body and sexual infantilism

Etiology—The fundamental defect in pituitary dwarfism is deficiency of anterior pituitary growth hormone There may be a congenital or idio pathic insufficiency of the acidophile cells or the condition may result from an injury to these cells from disease of the surrounding structures The most common causes of pituitary dwarfism are the *craniopharyngiomas* and other types of neoplasm *pituitary infarction* and *intracranial infec*

from hypophyseal disease is probably a primary disturbance of *hypothalamic function* with secondary alterations in endocrine activity

Etiology—Frohlich s syndrome is usually due to *craniopharyngioma suprasellar meningiomas chromophobe adenomas* of the *pituitary encephalitis* affecting the hypothalamic nuclei or *syphilitic basilar meningitis* In some cases there is no demonstrable organic basis for the syndrome

Pathogenesis.—Frohlich s syndrome was originally regarded as a manifestation of anterior pituitary insufficiency This concept received experimental support from the frequent occurrence after hypophysectomy of marked adiposity and genital hypoplasia In 1930 Smith demonstrated that some of the changes attributed to hypophysectomy were due actually to *hypothalamic injury* Careful removal of the hypophysis without trauma to the hypothalamus failed to produce adiposity Subsequent studies showed that hypothalamic injury particularly in the region of the tuber cinereum results in marked adiposity In contrast to the normal amount of adipose tissue amounting to one-seventh of the body weight an animal with an injury of this type may have one half its weight composed of fat It is now generally held that the Frohlich type of obesity is hypothalamic rather than hypophyseal

The regressive genital changes are in all likelihood due to a hypothalamic lesion Stimulation of the hypothalamus results in ovulation an increased secretion of gonadotropic hormone and pubertas praecox" which in many respects is the antithesis of Frohlich s syndrome These findings suggest that the hypothalamus regulates the release of gonadotropic hormone from the anterior pituitary and may give rise to hypergonadism or hypogonadism by variations in its functional activity In Frohlich s syndrome the hypothalamic defect may result in a failure to liberate pituitary gonadotropic hormone with resultant genital hypoplasia The skeletal retardation seen in juvenile forms of the syndrome according to the same reasoning represents an interference with normal release of growth hormone

In summary Frohlich s syndrome may be regarded as a disorder of hypothalamic and hypophyseal integrations leading to an interference with the normal release of anterior lobe secretions When the syndrome is caused by an expanding intracranial lesion there is a concomitant hypopituitarism which may culminate in an extreme degree of destruction as in Simmonds disease

Clinical Manifestations—The essential features of Frohlich s syndrome are obesity genital hypoplasia and faulty skeletal development

Obesity—Obesity is an early manifestation with localized deposits of fat about hips upper thighs lower abdomen mons pubis and breasts the face neck arms hands and legs being relatively free from fat There are large lipomatous masses in the areas mentioned giving rise to *macromastia* in females and a large panniculous adiposis The pattern of obesity is usually referred to as the female type The obesity is attended by a concomitant increase in total body weight

Genital Hypoplasia—In the juvenile form the genitalia fail to develop The penis scrotum testes and prostate retain their infantile size The secondary sex characteristics fail to appear the patient remaining a child sexually In adults there is loss of sexual function absence of libido and potentia amenorrhea sterility and frigidity Regressive changes occur in the genitalia and sexual characteristics In males the voice becomes high pitched and effeminate and gynecomastia is often pronounced

Skeletal Changes—The skeletal changes vary with the age of onset In adults when skeletal growth is complete abnormalities are not observed In children skeletal development is retarded or arrested due to failure of normal epiphyseal growth This results in shortening of the extremities genu valgum and a girdle type of obesity The cranial vault shares in the general osseous hypoplasia and is underdeveloped with a

normal but frequently protruding tongue The skin is soft at first but later becomes dry and scaly The head is flat in the occipital regions and the fontanelles close normally The extremities are normal but small Growth is stunted but the temperature pulse respiration and eliminative functions are normal The child is apt to be sleepy and quiet later he develops an animal like imitative faculty

See *Differential Diagnosis of Decreased Growth* (p 693)

Most Mongolian idiots have *congenital anomalies* such as cardiac malformations hernias clubfeet hydrocephalus The child usually succumbs before puberty and rarely survives beyond the twenty fifth year

Treatment—The management of the Mongolian idiot is by *institutionalization* Attempts to care for these children at home usually strain



Fig 243—Mongolian idiocy Note slanting eyes well developed epicanthic fold and open mouth

the resources of the family to the detriment of all particularly other growing children in the household

Laurence Moon Biedl Syndrome

The Laurence Moon Biedl syndrome is likewise included with the pituitary dysfunctions for want of more accurate information The disturbance has several distinctive cardinal features which include *retinitis pigmentosa obesity hypogenitalism mental retardation polydactylism* and a *familial history*

Nothing is known concerning the origin of this condition The prognosis is bad and therapy holds no promise

See *Differential Diagnosis of Decreased Growth* (p 693)

Anterior Pituitary Deficiency in Adolescence (Frohlich s Syndrome Adiposo genital Dystrophy)

The triad of obesity genital hypoplasia and retarded skeletal development formerly considered a form of anterior lobe insufficiency resulting

Lyon and Kaltenbach Mitchell s Pediatrics and Pediatric Nursing

from hypophyseal disease is probably a primary disturbance of *hypothalamic function* with secondary alterations in endocrine activity

Etiology—Frohlich's syndrome is usually due to *craniopharyngiomas suprasellar meningiomas chromophobe adenomas* of the *pituitary encephalitis* affecting the hypothalamic nuclei or *syphilitic basilar meningitis* In some cases there is no demonstrable organic basis for the syndrome

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The regressive genital changes are in all likelihood due to a hypothalamic lesion Stimulation of the hypothalamus results in ovulation an increased secretion of gonadotropic hormone and pubertas praecox which in many respects is the antithesis of Frohlich's syndrome These findings suggest that the hypothalamus regulates the release of gonadotropic hormone from the anterior pituitary and may give rise to hypergonadism or hypogonadism by variations in its functional activity In Frohlich's syndrome the hypothalamic defect may result in a failure to liberate pituitary gonadotropic hormone with resultant genital hypoplasia The skeletal retardation seen in juvenile forms of the syndrome according to the same reasoning represents an interference with normal release of growth hormone

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Obesity—Obesity is an early manifestation with localized deposits of fat about hips upper thighs lower abdomen mons pubis and breasts the face neck arms hands and legs being relatively free from fat There are large lipomatous masses in the areas mentioned giving rise to *macromastia* in females and a large panniculous adiposis The pattern of obesity is usually referred to as the female type The obesity is attended by a concomitant increase in total body weight

Genital Hypoplasia—In the juvenile form the genitalia fail to develop The penis scrotum testes and prostate retain their infantile size The secondary sex characteristics fail to appear the patient remaining a child sexually In adults there is loss of sexual function absence of libido and potentia amenorrhea sterility and frigidity Regressive changes occur in the genitalia and sexual characteristics In males the voice becomes high pitched and effeminate and gynecomastia is often pronounced

Skeletal Changes—The skeletal changes vary with the age of onset In adults when skeletal growth is complete abnormalities are not observed In children skeletal development is retarded or arrested due to failure of normal epiphyseal growth This results in shortening of the extremities genu valgum and a girdle type of obesity The cranial vault shares in the general osseous hypoplasia and is underdeveloped with a

shortening of the distance between the eyes a malformed sella turcica delayed secondary dentition, malformed and malposed incisors and maxillary prognathism Epiphyseal disorders usually due to some vascular disturbance are common and give rise to manifold orthopedic problems such as *Legg Perthes* (p 2927) and *Osgood Schlatter s diseases* (p 2929) The poorly developed facial bones create an infantile doll like appearance The fingers are delicate and tapering

The Skin—The skin is soft thin and transparent The nail crescents are often absent There is a definite hypotrichosis with sparse pubic and



Fig 244—Preadolescent hypophyseal insufficiency in a male

axillary hair and a hairless face in males Pigmented moles hemangiomas and fibrous moles are common Pigmentary spots appear as walnut colored stains in rounded areas

Intracranial Signs—The frequency with which the syndrome is produced by intracranial tumors and lesions accounts for the high incidence of neurologic symptoms and signs Choked disks optic atrophy oculomotor palsies and visual field defects are common Epileptiform seizures associated with an olfactory aura the so called uncinate fits' are not infrequently observed and result from the pressure of a tumor on the

* Cushing, after Neurath

uncinate gyrus Somnolence and narcolepsy are frequent findings especially in the encephalitic cases and reflect widespread hypothalamic change A classical description of narcolepsy as a manifestation of Frohlich s syndrome is the fat boy of Dickens Pickwick Papers As a rule the mentality is dull and sluggish The patient s reactions are slow and languid Intelligence is apt to be retarded It is not uncommon to find many of the features of the syndrome in patients with Parkinsonism Hypothermia has frequently been observed

Laboratory Data—The *metabolic changes* resemble those of hypopituitarism sugar tolerance is increased and spontaneous hypoglycemia is not infrequent the basal metabolic rate is usually reduced but not as markedly as in Simmonds disease (p 1169) The incidence of *diabetes insipidus* is high due to the anatomic proximity of the hypothalamic centers regulating water metabolism A mild *anemia* is usual as well as a moderate *lymphocytosis* and *eosinophilia*

X *rays* of the skull frequently indicate the presence of an intracranial lesion Studies of bone development show a delay in epiphyseal closure and in the appearance of ossification centers in juveniles and adolescents

Treatment —The treatment of Frohlich s syndrome depends to a great extent on the nature of the causative lesion If an intracranial tumor can be demonstrated *surgical ablation* is indicated especially if there is evidence of visual impairment Surgery is usually combined with *roentgenotherapy* which is also utilized when operative intervention is contraindicated

With idiopathic and postencephalitic lesions *rigid dietary control* leading to weight loss often produces marked improvement in general well being and genital function The development of the sex organs is stimulated by the use of *anterior pituitary* and *chorionic gonadotropic factors* *Thyroid extract* and *testosterone* are used with caution in juveniles since they favor premature epiphyseal closure

Anterior Pituitary Deficiency in the Adult (Simmonds Disease)

A marked diminution in the functional activity of the anterior pituitary gland results in a state of general physical and mental deterioration known as Simmonds disease The condition is characterized by extreme asthenia progressive emaciation and loss of sexual capacity

Etiology—Simmonds disease is caused by the gradual destruction of the adult anterior pituitary gland The factors responsible for the pituitary lesion are poorly understood In females *pregnancy* seems to bear a close etiologic relationship A history of repeated child bearing in rapid succession is not uncommon and suggests that the disease results from functional exhaustion of the gland Many instances of the disease have been observed in women who suffered from *postpartum hemorrhage* and *sepsis* According to Sheehan in these cases a sudden reduction in the blood supply to the gland incident to the collapse associated with postpartum hemorrhage precipitates ischemic thrombosis of the pituitary vessels with resultant infarction See p 115[illegible]

Occasionally the disorder is seen as a complication of an *infection* involving the *central nervous system* Hypophyseal damage has resulted from tuberculosis syphilis epidemic encephalitis bacterial meningitis and chronic pulmonary suppurations Other causative factors include intracranial trauma primary and metastatic brain tumors and the too successful removal of a craniopharyngioma or a pituitary chromophobe adenoma It occurs also as a late event in *acromegaly* when the pituitary inadequacy is superimposed on the antecedent hyperpituitarism In some patients there is no detectable cause for the deficiency of the an

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Occas onally the disorder is seen as a complication of an i *fection* involving the *central nervous system* Hypophyseal damage has resulted from tub rculosis syphilis ep demic encephalitis bacterial men ngitis and chronic pulmonary suppurat ons Other causat ve factors include intracranial trauma primary and metastat c bra n tumors and the too successful removal of a cran opharyngioma or a pituitary chromophobe adenoma It occurs also as a late event in *acrom galy* when the pitu tary inadequacy is superimposed on the anteced nt hyperpituitarism In some patients there is no d tectable cause for the defi ency of the an

terior lobe and there has been some indication that these idiopathic examples may result from *chronic inanition* which depresses the anterior pituitary and subsidiary members of the endocrine system The importance of this relationship is emphasized by the striking clinical resemblance between *Simmonds disease* and *anorexia nervosa* It is highly probable that many of the clinical features of Simmonds disease are actually the result of the inanition produced by the anorexia

Pathology—Autopsy in most cases discloses marked destruction or atrophy of the cellular elements of the anterior pituitary gland There is considerable variation in the amount of remaining glandular tissue Simmonds disease has been seen in the presence of a normal gland In some cases almost the entire lobe is replaced by fibrous or tumor tissue whereas others are afflicted with the disease despite the presence of 25 to 35 per cent of the gland Apparently the tempo of the destructive process must be slowly progressive to allow the syndrome to develop Sudden massive necrosis of the anterior lobe rapidly leads to collapse and death before symptoms are manifest

In women the lesion leading to replacement fibrosis of the secretory elements of the adenohypophysis is generally believed to be vascular According to Sheehan, necrosis results from involution and small vessel thrombosis the latter being incited by profuse postpartum *bleeding* Simmonds believed that the basic injury to the gland was postpartum embolization leading to infarction since the vessels of the anterior lobe are end arteries The great variety of destructive processes which have been found responsible include miliary tuberculosis sarcoidosis syphilis meningitis metastatic carcinomas secondary abscesses intracranial injuries primary meningiomas cysts arising from Rathke s pouch and encroaching upon the sella xanthomas and malignant gliomas

The extrapituitary lesions are widespread and consist essentially of atrophic changes These are especially prominent in the other members of the endocrine system There is marked atrophy of the parenchymal elements and fibrosis of the thyroid parathyroids pancreas adrenal cortex and gonads The viscera are small and atrophic a condition termed "splanchnomicria" There is usually evidence of marked emaciation with extensive loss of fat deposits The sweat glands and hair follicles are atrophic Some degree of pulmonary tuberculosis usually healed apical disease is frequently found

Pathogenesis—The modern concept of anterior pituitary function emphasizes the trophic role of the gland with respect to the secretory activity of the other endocrine organs The pioneer work of Smith showed that hypophysectomy resulted in atrophy of the thyroid parathyroids adrenal cortex and gonads Pituitary ablation is attended by anorexia failure of growth and development weight loss splanchnomicria and early senility These changes can be reversed in a few days by pituitary implants or by injections of crude anterior lobe extracts Experiments of this type have assigned to the anterior lobe the position of the master gland responsible for maintaining the functional capacity of the rest of the hormonal system

In this light Simmonds disease is a state of pluriglandular insufficiency arising from a primary deficiency of the tropic hormones of the anterior lobe The various clinical phenomena are attributable to a lack of the thyrotropic gonadotropic and adrenotropic factors and to the unopposed activity of the posterior lobe which gives rise to a characteristic disturbance of water metabolism

That this explanation may be too simple is indicated by the fact that the disease may occur in the absence of any pathologic changes in the pituitary Moreover patients with complete destruction of the anterior lobe may fail to evidence the typical clinical picture

Clinical Manifestations—Simmonds disease is rare and its onset is usually gradual A period of several years of vague ill health often elapses before the diagnosis is established The common antecedent events are postpartum hemorrhage infections and head injuries During the puerperium the first evidences of the disease are a *suppression of lactation* and periods of *extreme weakness* These are followed by rapid involution of the uterus atrophy of the external genitalia loss of libido and failure of menstruation to return

The complete clinical picture requires months or even years to develop and the principal symptoms are *anorexia asthenia loss of weight* sexual

debility and mental changes Marked weakness is noted by almost all patients and is particularly severe when the course of the disease is short As in the Addisonian patient (p 1271) there is a marked degree of *muscle adynamia* which prevents even light work

Loss of appetite and an intense dislike for food are usually present The result is a progressive loss in weight which in turn leads to a state of general emaciation More than 50 per cent of the average weight may be lost in a few years A fair number of patients may preserve the appetite for long periods and maintain a fairly normal state of nutrition

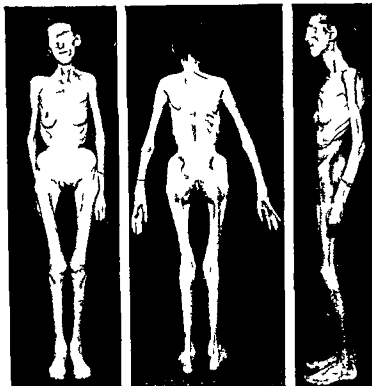


Fig 245—Hypophyseal cachexia (Simmonds disease) Single woman age 29 in terminal stages of disease Weight 49 lbs after loss of 82 lbs in three years Amenorrhea associated with atrophic genitalia and negative estrogen tests Anorexia Hypotension hypothermia, hypoglycemia and low basal metabolic rate (—40) Note extreme emaciation and loss of pubic hair

See *Differential Diagnosis of Loss of Weight* (p 700)

Amenorrhea is an early and constant symptom in females who may have noted a prolonged period of scanty irregular menses before the cessation of periodic bleeding In both sexes there is loss of libido and potency *Fertility* is impaired or lost but if pregnancy should occur there is apt to be marked improvement and even a complete cure of the Simmonds disease

Patients with Simmonds disease are very *sensitive to cold* as a result

of a fundamental defect in temperature regulation and depression of the basal metabolic rate *Blurring of vision* and *loss of visual acuity* occur when the anterior lobe hypofunction is caused by an intracranial neoplasm or granuloma

Mental disturbances may dominate the clinical picture Apathy dullness drowsiness confusion disorientation and depression are frequently encountered There may be a well marked Korsakoff s syndrome (p 1385) Instances of mania and marked *catatonia* have been reported Many of these psychic phenomena are clearly related to chronic hypoglycemia and are exaggerated by the hypoglycemic seizures The latter may be sufficiently severe to produce coma

Physical Examination—There is considerable variation in the general appearance of patients with Simmonds' disease Most patients appear *prematurely senile* the skin is wrinkled dry, inelastic and yellowish the teeth decay and fall out and the lower jaw is atrophic Axillary and pubic hairs are sparse There is an extreme degree of emaciation which exceeds that found in any other condition A striking absence of the adipose tissue of the gluteal areas is a common finding This appearance is usually associated with invalidism, marked loss of weight and severe general symptoms

Less typically emaciation is absent and a fairly good nutritional status is maintained The skin is dry and scaly and there is a tendency toward a diffuse subcutaneous thickening The head hair is dry and thin the eyebrows are thin and sometimes completely lost The clinical picture may be indistinguishable from a *primary myxedema* (p 1193)

In both sexes, the *external genitalia* are small and atrophic In the female *the labia are small and shriveled the uterus is infantile* and the breasts are markedly atrophic In the male the penis and the testes are small and the prostate gland may not be palpable

Cardiovascular abnormalities are common A *bradycardia* of 50 to 60 beats per minute is frequent the heart sounds are of poor quality and the heart is small The blood pressure tends to be low and may average 80 to 90 systolic and 50 to 60 diastolic *Orthostatic hypotension* (p 916) with postural symptoms is regarded as a pathognomonic sign of insufficiency *of the anterior lobe A similar postural circulatory difficulty* is also seen in Addison s disease In both conditions defective vascular adaptation to change in posture may be related to hypofunction of the adrenal cortex

Laboratory Findings—Studies of water exchange in patients with Simmonds' disease have disclosed the frequent presence of *oliguria* and delayed diuresis after water ingestion There is some evidence of an abnormal degree of sensitivity to the *antidiuretic* action of posterior lobe extracts Occasionally, *diabetes insipidus* has been observed and probably is the result of an injury to both lobes of the pituitary and the hypothalamus *Edema* is occasionally seen due to an excessive water retention or hypoproteinemia

A *low basal metabolic rate* is a constant finding in patients with Simmonds disease and may fall to the levels of a severe myxedema The hypometabolism is due to a deficiency of the calorigenic factor of the thyroid and malnutrition *Hypoglycemia* and an increased carbohydrate tolerance are usually present at some time Fasting hypoglycemia is common and

the oral glucose tolerance curve is usually flat There is an increased sensitivity to insulin and a decreased hyperglycemic response to epinephrine Hypoglycemic seizures are common and frequently lead to coma The disturbances in carbohydrate metabolism are similar to those observed in Addison s disease and are probably due to a deficiency of cortical carbohydrate factors

The *plasma cholesterol* remains normal or is moderately elevated even with advanced cachexia The serum chloride concentration is frequently low and there may be a negative chloride balance *Hypoproteinemia* is occasionally present and the urinary excretion of *17 ketosteroids* is markedly decreased suggesting a low output of adrenal cortical and gonadal hormones

A mild *anemia* usually hypochromic is almost always present and an *eosinophilia* is often noted *Achlorhydria* and *achylia gastrica* are frequently present The secretion of hydrochloric acid may be improved by the administration of thyrotropic hormone Low voltage in all leads is a frequent *electrocardiographic* finding *Osseous changes* are usually absent except in the region of the sella turcica Skull plates may show evidence of enlargement destruction or calcification of the sella

Course—Simmonds disease runs a slowly progressive downhill course A period of ten or fifteen years frequently elapses between the onset and termination Occasionally the tempo is rapid and death results in a few months or within a year The common mode of exitus is *coma* which is usually preceded by a short period of mental confusion convulsions and muscle rigidity During coma the pulse rate is slow and a hypothermia of 94° to 95 F may be present In other cases however coma is attended by hyperpyrexia

In most instances the coma is hypoglycemic in origin and may be relieved by intravenous dextrose The onset is commonly precipitated by severe anorexia and vomiting an intercurrent illness or an insufficient food intake Coma which is not attributable to hypoglycemia is ascribed to cerebral changes incident to severe malnutrition avitaminosis and hormonal deficiencies Some patients die from other causes such as a complicating pulmonary tuberculosis

Diagnosis—The diagnosis of Simmonds disease is difficult since there is very little in the clinical picture that is not encountered in a great variety of fairly common conditions Deterioration of pituitary origin must be differentiated from the cachexias due to *tuberculosis malignancy* and *hyperthyroidism* Aside from obvious features of these last conditions the basal metabolic rate is almost always normal or elevated in contrast to the very low level of oxygen consumption in Simmonds cachexia In addition the former states are not usually attended by sexual involution of the degree seen in pituitary hypofunction

Addison s disease is usually considered as a possible diagnosis The close resemblance of the two conditions is readily understandable since the Simmonds patient is actually suffering from adrenal as well as pituitary insufficiency The distinction is easily made in the Addison s syndrome by the presence of the characteristic *brown pigmentation* In the absence of pigmentation chemical studies reveal the markedly increased urinary excretion of sodium which is characteristic of adrenal insufficiency

The most difficult problem in diagnosis is to differentiate between Simmonds disease and *anorexia nervosa* The occurrence of severe weight loss and a low basal metabolic rate in a young female who has never been pregnant and who has manifest psychopathic trends is highly suggestive of anorexia nervosa

Treatment—The treatment of Simmonds disease is disappointing The logical measures include the replacement of deficient hormones by the use of suitable extracts of the anterior lobe thyroid adrenal cortex and gonads

Therapy with *anterior pituitary extracts* has been difficult to evaluate in view of the doubtful status of the diagnosis Injections of *thyrotropic factor produce* a temporary increase in basal metabolic rate with a subsequent fall to original levels improvement in gastric acid secretion and in general well being

When the clinical manifestations resemble those of a primary myxedema moderate doses of *thyroid extract* raise the basal metabolic rate *to normal and produce symptomatic improvement In some cachectic* patients it alleviates the loss of appetite and promotes a gain in weight The use of thyroid may precipitate vomiting which has been ascribed to an aggravation of the adrenal insufficiency *Ovarian hormone therapy* is disappointing as is treatment with crude *adrenal cortical extracts* The purified adrenal cortical steroids have not as yet been used in this group of patients

Pregnancy is the most helpful therapy for females During pregnancy there is a marked general improvement which is maintained after delivery *In all likelihood the benefit is due to the hypertrophy of the remnant* of functioning anterior lobe tissue

A *high carbohydrate diet* is best utilized and tends to protect against hypoglycemia Large amounts of *vitamins* are given particularly of thiamine chloride

Adiposis Dolorosa (Dercum s Disease)

Little is known concerning the pathogenesis of adiposis dolorosa The condition is here presented with the anterior pituitary disorders only because of its resemblance to the Frohlich and Cushing syndromes

The cardinal features of Dercum s disease are the presence of *painful fat deposits asthenia* and *mental deterioration* The condition is observed more often in women and is apt to occur at the time of the menopause The fat deposits resemble a 'caked breast and feel as though they were filled with a bundle of worms The pain and obesity result in marked asthenia and depression

See *Differential Diagnosis of Gain in Weight* (p 695)

The *prognosis* is bad since relief cannot be given and therapeutic endeavors are without avail A low calory diet with thyroid administration may be attempted but little improvement will be observed

CLINICAL ABNORMALITIES OF THE ANTERIOR PITUITARY

Pathologic abnormalities of the anterior pituitary gland have little significance except insofar as they are related to the clinical manifestations

of deranged physiology So far as is known the more frequent conditions include neoplasms inflammations and vascular derangements

Acidophile Adenomas —See *Gigantism* and *Acromegaly* (p 1158)

Basophile Adenomas —See *Cushing s Syndrome* (p 1159)

Carcinomas of the Pituitary Gland —See *Simmonds Disease* (p 1169)

Chromophobe Adenomas —Chromophobe adenomas constitute 70 per cent of all pituitary neoplasms Inasmuch as their cells have no known physiological activity the rapidly growing tumors give rise to syndromes of compression of the hypothalamus and optic chiasm There is an even

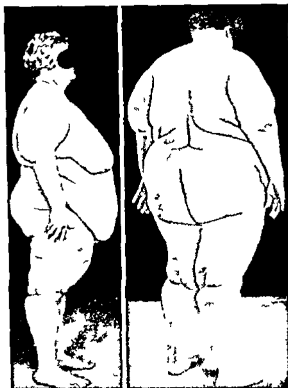


Fig 246 —Adiposis dolorosa (Dercum s disease) Patient 4 years of age W ght 327 lbs after ga n of 120 lbs in two ye rs Amenorrhea asthenia nervou and psychic mani f stati ns and t n ler f t depo ts

tual pressure atrophy of the actively functioning elements of the gland with the inevitable development of pituitary insufficiency

P thol gy —The tumors are soft fri ble masses of poorly sta ning chromophobe cells co taining a clear cyt plasm Th y grow rap dly eroding the bony sella which is sym metric lly enlarged often to great size (ballooning) There is ma ked eros on of the thin cl noid proce ses and the equally th n sphenoid base which may rupture following extension of the growth nto the sph o lal sinuses The up a d growth of the tumor leads to com press on of the i inferior po t on of each opt c nerve and a gradu l pressu e atrophy of th inner fibers of the opt c nerves Th hypothalamus is invariably compressed The t mors may ext nd l terally to involve the tempo al lobe and the oculomotor nerves The

remnant of the normal gland is usually a flattened crescent of tissue containing a few scattered acidophils and basophils The extracranial lesions are similar to those encountered in hypopituitarism from other causes

See *Anterior Pituitary Insufficiency* (p 1164)

Clinical Manifestations —Chromophobe tumors are seen commonly in adults between the ages of thirty and fifty This is in sharp contrast to the frequency of *craniopharyngiomas* in children Both sexes are equally affected

The symptoms and signs are the result of *progressive mechanical pressure* on neighboring structures Of the neurologic manifestations *head-*



Fig 247 —Two children of the same age The one on the right is normal The one on the left developed a craniopharyngioma at the age of five Note the complete cessation of growth *

ache is an early symptom It may be frontal or bitemporal and the patient usually localizes it behind the eyeballs The headache increases in severity with the growth of the tumor within the unyielding sella but may disappear eventually when the growth breaks through the diaphragm into the cranial cavity

Visual difficulty results from involvements of the chiasm and optic nerves As in acromegalics there is a *bitemporal visual field defect* be

* Ray and Heuer in Cecil Textbook of Medicine

ginning in the upper outer quadrants and extending downward until there is a *bitemporal hemianopsia* Later there may be complete *blindness* Fundus examination reveals a typical *primary optic atrophy* *Choking of the disk* may be seen with very large tumors that interfere with the free passage of fluid through the foramen of Munro There may be choking of the disk on one side with optic atrophy on the other Compression of the hypothalamus leads to *hypothermia* disturbances of the sleep rhythm (*hypersomnolence* or *narcolepsy*) and in young adults a tendency to *obesity*

The *endocrine features* are those of *anterior lobe insufficiency* Depending on the age of the patient there may be *pituitary dwarfism* (p 1164) *adiposogenital dystrophy* (p 1166) or *Simmonds disease* (p 1169)

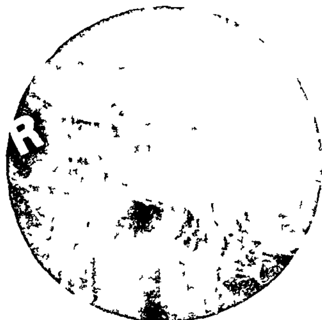


Fig 248—Typical appearance of the sella turcica in adenoma Balloon shaped enlargement pointing of the anterior clinoids thinning of the dorsum sellae turcicae and encroachment on the sphenoid sinus

Treatment—*Surgical removal* of pituitary tumors by transfrontal approach through the anterior cranial fossa has a 10 per cent mortality in the best hands Roentgen therapy which avoids the surgical risk is tried first with eventual resort to surgery if a remission does not occur or if there is evidence of progressive compression of the optic pathways There may be a temporary exaggeration of headache and visual difficulty during irradiation probably as a result of edema of the tumor This subsides within a few days The treatment of hypopituitarism is carried out according to the principles outlined in the section on Simmonds disease (p 1169)

Craniopharyngiomas—The craniopharyngioma arises from the embry

onic Rathke s pouch which is an outgrowth of the epithelial lining of the oral cavity The osseous closure of the sphenoid bone in the third month of embryonic life pinches the pouch off from the epithelial stalk leaving an intracranial cell nest

Pathology—Craniopharyngiomas arise from the continued growth of epithelial rests They vary in size from a small pea to growths of a large apple and expand into the floor of the third ventricle and the adjacent temporal lobes They lie above the sella and chiasm where because of their anatomical location they are known as *suprasellar cysts* The tumors vary in consistency from small solid growths to large multilocular cysts They are usually filled with *reddish brown oily fluid containing cholesterol crystals Calcification is common* and is sufficient to give evidence of suprasellar calcification on x ray Histologically the tumors are classed as *adamantinomas*

Clinical Manifestations—Because of its location a tumor of this type exerts pressure upon the *pituitary stalk* the *hypothalamus* the *optic chiasm* and the *hypophysis* The latter structure shows various degrees of injury varying from a scarcely detectable change to a complete atrophy of the parenchyma The clinical manifestations may be those of *pituitary*

TABLE 82—POSTERIOR PITUITARY LOBE PREPARATIONS

Product	Diluent	Alpha Hypoph amine activity (U S.P units per cc)	Beta Hypoph amine activity (U.S P units per cc)	Remarks
Posterior Pituitary Injection U.S P (Pituitrin)	Water	10	10	Standard preparation
Pitocin N N R	Water	½	10	For oxytocic activity
Pitressin N N.R	Water	20	1	For pressor and anti diuretic responses
Pitressin Tannate N N.R	Oil	5		For prolonged anti diuretic response

dwarfism (p 1164) or the *adiposogenital syndrome* (p 1166) Less often *craniopharyngiomas produce Simmonds disease* (p 1169) The principles of treatment are those discussed under *chromophobe tumors* (p 1175)

Atrophy of the Anterior Pituitary Gland—See *Adrenal Cortical Deficiency* (p 1271)

Hyperplasia of the Anterior Pituitary Gland—See *Pituitary Acidophilism* (p 1153) *Pituitary Basophilism* (p 1164)

Vascular Injuries—The acute manifestations of Simmonds disease noted in relationship to *pregnancy* are thought to result from infarction of the anterior pituitary blood supply with subsequent death of tissue and the development of *anterior pituitary deficiency* (p 1169)

THE POSTERIOR PITUITARY GLAND

Anatomy—See p 1152

Histology—See p 1153

Pharmacology—Extracts of posterior lobe pituitary possess at least two distinct pharmacologic entities *beta hypophamine* has the effects of ele

vating blood pressure through stimulation of smooth muscle and of exerting a diuretic antidiuretic influence through alteration in the reabsorption of water by the renal tubules *alpha hypophamine* has almost exclusively oxytocic activity producing active contraction of the uterus

Assay and Preparations—Posterior pituitary preparations are assayed according to standards established by the United States Pharmacopeia Each U.S.P unit represents the activity of 0.5 mg of the U S P posterior pituitary reference standard The unitage applies to pressor oxytocic and anti diuretic activities although only the oxytocic activity is actually assayed on the isolated virgin guinea pig uterus

TABLE 82A—DIAGNOSTIC AND THERAPEUTIC ACTIONS OF POSTERIOR PITUITARY PREPARATIONS

Antidiuresis

Specific effect in diabetes insipidus best obtained by use of Pitressin Tannate in Oil may also be induced by intranasal instillation of posterior pituitary extract or powder

Pressor response

Intramuscular injection of pitressin produces rise in blood pressure within 1 to 2 minutes lasting from 10 to 30 minutes

More intense responses may produce coronary insufficiency angina pectoris and collapse

Oxytocic effect

Intramuscular injection of pitocin produces direct stimulation of myometrium small doses augment tone and increase amplitude of uterine contractions but larger doses may cause tetanic spasms administration not without danger unless cervix is fully dilated best used after expulsion of placenta in the prevention of postpartum hemorrhage and uterine atony See p 2717

Stimulation of gastro intestinal musculature

Intramuscular injections of pitressin are utilized in prevention and relief of paralytic ileus particularly following operation pituitary preparations neither as reliable nor as free from side-effects as neostigmine (p 1851) which is preferred for this purpose

Tests of renal function

Intramuscular injections of pitressin produces decrease in urine volume and increase in urine specific gravity as in water tests for concentration and dilution (p 2240)

Epilepsy tests

Epileptic seizure may be induced for diagnostic purposes by the simultaneous administration of large quantities of fluid and hourly doses of pitressin as described in greater detail in the discussion of Epilepsy (p 1516)

Miscellaneous

Intramuscular injections for assistance in the expulsion of ureteral calculi and for the relief of pain in herpes zoster

Besides these important pharmacologic actions the posterior pituitary products also produce depression of oxygen consumption an anti insulin action resulting in hyperglycemia depression of the renal reabsorption of sodium potassium and chloride ions and stimulation of frog melanophores causing pigmentary changes

Therapeutics—Posterior pituitary extracts are employed in clinical medicine for specific substitution effects in diabetes insipidus for pharmacologic reactions through stimulation of smooth muscles in the arteries intestinal tract and uterus and for diagnostic tests for renal function and in epilepsy

Toxicity—The administration of a potent posterior pituitary extract is not devoid of danger The pressor activity is a variable an intense vaso

onic Rathke s pouch which is an outgrowth of the epithelial lining of the oral cavity The osseous closure of the sphenoid bone in the third month of embryonic life pinches the pouch off from the epithelial stalk leaving an intracranial cell nest

Pathology —Craniopharyngiomas arise from the continued growth of epithelial rests They vary in size from a small pea to growths of a large apple and expand into the floor of the third ventricle and the adjacent temporal lobes They lie above the sella and chiasm where because of their anatomical location they are known as *suprasellar cysts* The tumors vary in consistency from small solid growths to large multilocular cysts They are usually filled with reddish brown oily fluid containing cholesterol crystals Calcification is common and is sufficient to give evidence of suprasellar calcification on x ray Histologically the tumors are classed as *adamantinomas*

Clinical Manifestations —Because of its location a tumor of this type exerts pressure upon the *pituitary stalk* the *hypothalamus* the *optic chiasm* and the *hypophysis* The latter structure shows various degrees of injury varying from a scarcely detectable change to a complete atrophy of the parenchyma The clinical manifestations may be those of *pituitary*

TABLE 89 —POSTERIOR PITUITARY LOBE PREPARATIONS

Product	Diluent	Alpha Hypoph amine activity (U S P units per cc)	Beta Hypoph amine activity (U S P units per cc)	Remarks
Posterior Pituitary Injection U.S.P (Pituitrin)	Water	10	10	Standard preparation
Pitocin N N R	Water	½	10	For oxytocic activity
Pitressin N N.R	Water	20	1	For pressor and anti diuretic responses
Pitressin Tannate N N R	Oil	5		For prolonged anti diuretic response

dwarfism (p 1164) or the *adiposogenital syndrome* (p 1166) Less often craniopharyngiomas produce *Simmonds disease* (p 1169) The principles of treatment are those discussed under *chromophobe tumors* (p 1175)

Atrophy of the Anterior Pituitary Gland —See *Adrenal Cortical Deficiency* (p 1271)

Hyperplasia of the Anterior Pituitary Gland —See *Pituitary Acidophilism* (p 1153) *Pituitary Basophilism* (p 1164)

Vascular Injuries —The acute manifestations of Simmonds disease noted in relationship to *pregnancy* are thought to result from infarction of the anterior pituitary blood supply with subsequent death of tissue and the development of anterior pituitary deficiency (p 1169)

THE POSTERIOR PITUITARY GLAND

Anatomy —See p 1152

Histology —See p 1153

Pharmacology —Extracts of posterior lobe pituitary possess at least two distinct pharmacologic entities *beta hypophamine* has the effects of ele

mone on the renal absorption of water has been demonstrated most clearly there is also ev dence that the pars nervosa has other actions whose absence may contribute to the clin ical picture of diabetes insipidus The antidiuretic factor causes a variable temporary and inconstant increase in the urinary excretion of *sod um* and *chloride* This action is separable from the antid uretic effect and is opposite to the salt retaining action of adrenal cortical hormones indeed *a diabetes insipidus like condit on* may be induced by the administration of desoxycorticosterone acetate It is conceivable that the renal excretion of sodium is con trolled by an equilibrium between the two glands and that in the absence of the posterior lobe the tendency to retain sodium is enhanced

Clinical Manifestations —The cardinal symptoms of diabetes insipidus are *excessive thirst* and *polyuria* Associated with these are manifestations due to tissue dehydration the excessive loss of body heat and the under lying intracranial lesion

Thirst —Thirst is intense and is usually the chief complaint It is often difficult to relieve in spite of the drinking of tremendous quantities of water In about half of the patients the appearance of thirst is so sudden that the day of onset may be positively fixed In many cases thirst pre cedes the polyuria by several hours The patient may drink several quarts of water at one time and be unable to sleep because of the urge to drink The *insomnia* so produced quickly leads to *fatigue* and *depression.* Water restriction is poorly tolerated and constitutes an unbearable form of tor ture It quickly leads to nausea vomiting anhydrosis and an increase in body temperature if there is a high level of fluid exchange

The *mechanism* for the production of thirst is not thoroughly under stood It is not merely the result of excessive water loss since polydipsia and polyuria approximate each other Moreover after periods of moderate water restriction more water is consumed than is lost from the body Thirst may be related to a relative decrease in the ability to excrete sodium in the urine and thus is a reaction to hypernatremia The relation of sodium chloride to the syndrome is indicated by the marked increase in water exchange that occurs when salt is added to the diet of the patient with diabetes insipidus whereas in normal individuals a similar quantity of salt produces only comparatively slight changes in water bal ance Conversely the removal of salt from the diet often results in a dramatic decrease in polydipsia and polyuria but does not restore water exchange to normal

Polyuria —The ingestion of large quantities of fluid maintains a marked polyuria with a urine of low specific gravity Depending on the severity of the syndrome the urine volume may vary from a slight increase above the normal (3 liters) to tremendous volumes (60 liters) The patient may be in a state of constant water diuresis resulting in such *frequency* and *nocturia* as to confine him to his home The capacity of the bladder is increased and it is not uncommon for patients to pass a liter of urine at a single voiding

The urine is pale water clear and of *low specific gravity* (1 001 to 1 005) Water restriction is accompanied by a decrease in polyuria and a rise in urine specific gravity There is a negative water balance however and evidences of tissue dehydration develop rapidly

Manifestations Due to Tissue Dehydration —Despite the large fluid ex change and free access to water many patients present evidences of tis sue dehydration The *skin* is coarse and dry *sweating* is slight or may be

constriction may produce a rapid rise in blood pressure with cardiac pain pallor coronary insufficiency and circulatory collapse An occasional fatality has been experienced Excessive spasm of uterus or intestine may produce such violent cramping as to lead to syncope or rupture of the spastic viscus

DEFICIENCY OF THE POSTERIOR PITUITARY GLAND (DIABETES INSIPIDUS)

Diabetes insipidus is a disturbance of water metabolism and renal function It is caused by the failure of the *antidiuretic hormone* of the posterior lobe of the pituitary gland to exert its normal physiologic control over water exchange The principle clinical features are *extreme thirst* and marked *polyuria* In most instances these are controlled by replacement therapy with posterior lobe extracts

Etiology and Pathology—Diabetes insipidus may be produced by an actual deficiency in the antidiuretic factor of the posterior lobe *or by interference with the normal activity of* the hormone Patients who belong in the former category are easily controlled by replacement therapy with posterior lobe extracts and are designated as *pituitrin sensitive* Those in the second group which is rare are affected slightly by therapy and are termed *pituitrin resistant*

Pituitrin Sensitive Diabetes Insipidus—The elaboration of antidiuretic factor is controlled by a hypothalamic center and the supra-optic nuclei connected to the pars nervosa by the supra optico hypophyseal tract of nerve fibers Injury to any of the component parts of this system namely the supra-optic nuclei the tract or the posterior hypophysis may give rise to an insufficiency of the secretory elements of the gland A great variety of lesions about the base of the brain may affect the functional integrity of the hypothalamo hypophyseal system These include primary or metastatic tumors about the base of the brain and in the posterior cranial fossa syphilitic basilar meningitis tuberculous meningitis tuberculomas basilar skull fractures bullet wounds infectious processes after measles diphtheria pertussis scarlet fever chickenpox mumps erysipelas influenza typhoid malaria and encephalitis intracranial extension of an infection of the upper respiratory passages and essential xanthomatoses Diabetes insipidus occurs also in the absence of any definite organic lesion but with a hereditary familial basis

The disturbance of the hypothalamo hypophyseal complex leading to a decreased elaboration of the antidiuretic principle is not the only factor involved in the production and maintenance of diabetes insipidus Complete hypophysectomy does not produce the syndrome and normal anterior pituitary function seems essential for the development and maintenance of the syndrome although the exact relation of the anterior lobe to diabetes insipidus has not as yet been satisfactorily explained

Pituitrin-Resistant Diabetes Insipidus—Pituitrin resistant diabetes insipidus may be hypothalamic or endocrine in origin *The hypothalamic variety apparently results from the* destruction of the tuber cinereum due to *syphilitic basilar meningitis or epidemic encephalitis* Pituitrin resistant diabetes insipidus has been observed in association with endocrine disorders such as *acromegaly* and *Cushing's syndrome*

Pathogenesis—The fundamental defect in diabetes insipidus is the failure of the pars nervosa to exert its normal physiologic control over water exchange The exact nature of this control is a matter of conjecture but it obviously involves the regulation of the renal excretion of water and its distribution in the body The evidence indicates that the pituitary gland elaborates a hormonal *antidiuretic factor* which acts directly upon the kidney causing an accelerated reabsorption of water from the glomerular filtrate "In its absence about four fifths of the water in the glomerular filtrate are reabsorbed isomotically it is by the variable reabsorption of the remaining fifth under the influence of this hormone that the urine is raised to levels hypertonic to the blood and that the water content of the plasma is regulated (Smith) A lack of antidiuretic factor thus impairs the ability to elaborate a maximally concentrated urine producing a form of *hyposthenuria* and favoring the development of *polyuria* and *a negative water balance* The excessive water loss leads to thirst and the resultant *polydipsia* maintains the water exchange at high levels

Antidiuretic Hormone Versus Adrenal Cortical Hormone—While the effect of the hor

and longevity Some patients have the disease for more than forty years The intensity of the syndrome is usually increased by *pregnancy* and becomes less severe after the *menopause* In cases of a secondary nature the prognosis is that of the causative lesion and is poor with an intracranial neoplasm Patients with *essential xanthomatosis* (Schuller Hand Christian syndrome) usually succumb early to an intercurrent infection

The diabetes insipidus tends to vary in severity for reasons difficult to determine It may disappear entirely In cases due to neoplasm or infection this may indicate the complete destruction of the anterior lobe The erratic nature of the course makes it very difficult to evaluate the efficacy of therapeutic procedures

Treatment—The treatment of diabetes insipidus aims at control of polydipsia and polyuria and removal of the cause of the syndrome Obviously the efficacy of the latter depends on the nature of the pathologic process Neoplastic vascular inflammatory and traumatic lesions of the hypothalamohypophyseal system usually produce irreversible damage

Symptomatic Therapy—The symptoms of diabetes insipidus are adequately controlled in the majority of patients by replacement therapy with posterior lobe extracts containing the antidiuretic factor

PITRESSIN—The antidiuretic hormone is usually administered subcutaneously in the form of pitressin (alpha hypophamine) The doses vary with the severity of the disease and the pituitrin sensitivity of the patient In mild examples 0 5 cc daily usually given before bedtime is sufficient In more severe disturbances the hormone must be given every three or four hours night and day The use of pitressin hypodermically may be attended by severe abdominal cramps anorexia diarrhea and severe headache Some patients must be cautioned to restrict drinking since a continued large intake may cause excessive water retention and intoxication

PITRESSIN TANNATE—The disadvantages of aqueous preparations of antidiuretic factor have been largely eliminated by the use of a suspension of pitressin tannate in sesame oil Small doses of this preparation are effective in controlling polydipsia and polyuria They have a sustained action requiring only one injection every twenty four to forty eight hours A dose in excess of 0 25 to 0.30 cc of pitressin tannate in oil daily should not be continued unless the clinical condition of the patient is followed closely

The hormone is available in ampoules containing 5 pressor units per cc Since the active principle settles out of the oil vehicle the contents of the ampoule are shaken vigorously until a uniform suspension is obtained The contents are withdrawn through a needle of sufficient gauge (18 to 20) to prevent clogging No toxic effects are observed following the use of this preparation although excessive amounts quickly lead to symptoms of water intoxication At present *pitressin tannate in oil* is the most effective preparation available for the treatment of diabetes insipidus

NASAL APPLICATIONS—Antidiuretic factor also is given effectively by the application to the nasal mucosa of cotton pledgets soaked in an aqueous preparation or by the inhalation of powdered pituitary extract These forms of therapy have the great advantage of simplicity of administration but the hormone must be taken every two or three hours and untoward effects and local irritation are common

completely absent the *mouth* is dry the *lips* are cracked and the *mucosa* of the upper respiratory passages is thick and tenacious *Constipation* is common and is probably due to inspissation of stool These manifestations are intensified by water restriction

Manifestations Due to Excessive Heat Loss—In severe diabetes insipidus the drinking of large quantities of cold liquids imposes a considerable burden on the heat regulating mechanisms of the body As a result there is an *abnormal sensitiveness to cold* and the frequent occurrence of *subnormal body temperatures* To compensate for the heat loss the patient responds with bulimia polyphagia shivering peripheral vasoconstriction and increase of the basal metabolic rate

Manifestations Due to the Intracranial Lesion—Since diabetes insipidus usually is secondary to an intracranial disease process neurologic symptoms and signs are commonly encountered These may be of any variety and depend on the nature and extent of the process The common findings include visual field defects, progressive loss of visual acuity ocular palsies especially abducens paralysis pupillary inequalities bitemporal hemianopsia and papilledema In many instances there are associated evidence of hypothalamic disease such as *Frohlich s syndrome* (p 1166) *pubertas praecox* (p 2480) *infantilism* (p 1164), *hypersomnia* (p 1307) and *Parkinsonism* (p 1505)

Laboratory Findings—The blood count is usually normal but a slight polycythemia or a moderate secondary anemia may be observed

Blood Chemistry—There is considerable confusion regarding the chemical composition of the blood plasma in diabetes insipidus Peters states that there are no definite deviations from the normal in plasma composition but an increase in *serum sodium* concentration has been reported Moderate water restriction produces a sharp rise in serum *sodium* *The blood urea* is normal or more frequently low due to the constant diuresis *Blood volume* studies have failed to reveal any significant deviation from the normal despite the excessive exchange of fluid After pituitrin administration there is apparently a definite hemodilution

Renal Function—The nature of the functional renal defect in diabetes insipidus is an extremely interesting problem that remains to be satisfactorily solved The urine is of large volume with a low specific gravity (1 001 to 1 005) Fifty per cent of patients show traces of *albumin* from time to time and, with a complicating diabetes mellitus there is a *glycosuria*

Studies of renal function have failed to reveal any abnormalities of glomerular filtration On the other hand the ability to elaborate a concentrated urine is diminished and is reestablished to some extent by antidiuretic factor There is evidence that the ability to excrete sodium chloride is reduced Salts and urea are quantitatively excreted but in dilute form with an abnormally large volume of water During water restriction the urine specific gravity rises but remains below normal levels There is a decrease in the ability to concentrate chloride and urea which is associated with the retention of salt and urea in the blood

Course—The course and prognosis depend on the nature of the underlying process responsible for the production of the syndrome Idiopathic cases run a long benign course with little interference with general health

Macrogenitosomia Praecox —Those who develop signs between the ages of eighteen months and five years reveal unusually *enlarged stature* and the body configuration genitalia and hair distribution of the adult *Excessive sexual function* is attested by erections emissions masturbation and heterosexual attraction Those few females who are afflicted with the disease do not show corresponding changes

Increased Intracranial Pressure —In addition to specific clinical manifestations there are evidences of marked and progressive *internal hydrocephalus* Interference with the circulation of the cerebrospinal fluid through the aqueduct of Sylvius produces increase in intracranial pressure The patient complains of *headache* which is most often suboccipital *tenderness and rigidity of the neck vomiting* and *weakness* With continuation of pressure disturbances there is progressive *loss of vision* due

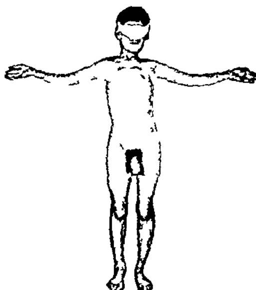


Fig 240 —Pubertas praecox of pineal origin in a boy ten years of age showing large genitals and profuse growth of pubic hair

to destruction of the optic chiasm and tracts or the quadrigeminal plates The later course is marked by paralyses of extra ocular muscles diabetes insipidus deafness loss of weight increasing stupor slowness of cerebration convulsions and coma Children who have shown sexual precocity in the earlier phases later become mentally and physically dull adults suffer sexual debility

Treatment —Pineal feedings are instituted by enthusiasts for endocrinologic therapy but there is no evidence that products have any potency When the condition is suspected the patient should be referred to a specialist in neurosurgery in the hope that enucleation can be successfully attempted

Courtesy of Dr Walter Timme from Lectures in Endocrinology published by Paul B Hoeber Inc

MISCELLANEOUS —Considerable symptomatic improvement follows the restriction of the intake of sodium chloride to 1 gm daily There is some evidence that a low intake of protein also is of value Repeated lumbar puncture and the use of phenobarbital, pentobarbital salicylates amino pyrine and sex hormones have been favorably reported but have no essential place in a long range schedule

'CURATIVE' EFFORTS —In certain instances a direct therapeutic approach has brought about a termination of the syndrome The results of such therapy must be interpreted guardedly since the syndrome may regress spontaneously The most impressive results have been obtained in syphilitic basilar meningitis treated by *antisyphilitic measures* In a few instances tumors have been successfully removed *surgically* with prompt relief of the polyuria and polydipsia

The beneficial effect of *pituitary irradiation* on the course of diabetes insipidus has been reported by several observers Deep x ray therapy to the sella turcica has been associated with improvement in diabetes insipidus due to essential xanthomatosis apparent cures have been reported in cases of inflammatory origin The limitations of x ray therapy are obviously great since therapeutic success depends on the potentialities of residual function of the pars nervosa

PINEAL GLAND

The importance of the pineal gland has been variously estimated by investigators Descartes believed it to be the seat of the soul , more modern opinion is inclined to the concept that the organ is vestigial

Anatomy —The pineal gland lies at the posterior and superior extremity of the third ventricle It is situated between the splenium of the corpus callosum and the corpora quadrigemina Its measurements in the adult approximate 7 x 4 mm When calcified it is demonstrable on radiographs but it is otherwise inaccessible to clinical examination Microscopically there are characteristic parenchymal cells varying amounts of neurological substance and a few nerve and blood elements

Physiology —Those who are skeptical about the functions of the pineal body regard the structure as a *rudimentary third eye* and cannot assign any functional significance to the organ Against this negative view are experimental and clinical findings which suggest that the gland may have some importance under certain conditions in *relation to sexual growth*

CALCIFICATION OF THE PINEAL

Calcification of the pineal is an occasional finding on routine *radiography* of the skull The condition is unassociated with any consistent clinical manifestations and requires no therapy

NEOPLASMS OF THE PINEAL

Tumors of the pineal are relatively rare but *pinealomas pineoblastomas* and *teratomas* have been described

Clinical Manifestations —Most pineal tumors occur in males the majority of those afflicted develop symptoms prepuberally and exhibit nonspecific evidences of increased intracranial pressure and the more definitive and localizing syndrome of precocious puberty (Pellizzi syndrome macrogenitosomia praecox) or pituitary basophilism (p 1159) It is generally believed that these syndromes are due to pressure of tumors on the mesencephalon and are essentially hypothalamic in origin

Macrogenitosomia Praecox—Those who develop signs between the ages of eighteen months and five years reveal unusually *enlarged stature* and the body configuration genitalia and hair distribution of the adult *Excessive sexual function* is attested by erections emissions masturbation and heterosexual attraction Those few females who are afflicted with the disease do not show corresponding changes

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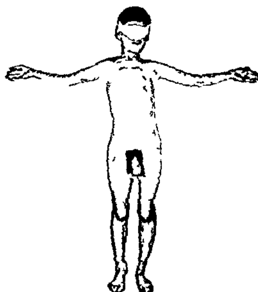


Fig. 219—Pubertas praecox of pineal origin in a boy ten years of age showing large genitals and profuse growth of pubic hair *

to destruction of the optic chiasm and tracts or the quadrigeminal plates The later course is marked by paralyses of extra ocular muscles diabetes insipidus deafness loss of weight increasing stupor slowness of cerebration convulsions and coma Children who have shown sexual precocity in the earlier phases later become mentally and physically dull adults suffer sexual debility

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CHAPTER 57

THE GLANDS OF THE NECK AND CHEST THYROID PARATHYROIDS CAROTID BODY THYMUS

THE THYROID GLAND

THE thyroid is the only ductless gland that is visible and palpable These features have facilitated methods of study and simplified many diagnostic and therapeutic problems

Anatomical Considerations—The human thyroid is a bilobed butterfly shaped structure situated in the lower third of the anterior cervical region The roughly pyramidal *lateral lobes* about 5 x 2 cm are joined by an *isthmus* which lies anterior to the second and third tracheal rings The gland is invested by a thin transparent layer of fibrous tissue which is closely applied to the parenchyma The outer or surgical capsule binds the gland to the trachea so that the thyroid moves with swallowing The *pyramidal process* a tongue like projection often extends upward to connect with the remnant of the embryonic *thyroglossal duct*

The adult thyroid weighs about 20 gm It is slightly larger in the female and is subject to changes in size and shape in response to climatic geographic nutritional and physiologic influences *Accessory thyroid tissue* may be found at the base of the tongue in the mediastinum along the thyroglossal duct and in the cervical tissues The close anatomical proximity of the gland to the *larynx trachea* and *inferior laryngeal nerves* results in disturbances due to the mechanical pressure of an enlarged goiter or injury as a result of thyroid surgery

The thyroid gland is extremely vascular It receives large superior and inferior branches from the external carotid and subclavian arteries the smaller thyroid ima from the arch of the aorta and a rich collateral circulation from the tracheal laryngeal and esophageal vessels

On microscopic section the gland consists of follicles lined with single layers of cuboidal or columnar epithelial cells and a supporting stroma of reticular connective tissue. The follicles contain a viscid homogenous *colloid* material which stains with eosin and stores the iodine containing thyroid hormone.

Physiology — The thyroid hormone seems profoundly to affect the life of the cell in every major aspect of its existence: its physical state, its chemical state, its irritability, its rate of maturation and the rate at which it undergoes mitosis, that is to say, the length of its life. . . . The hormone retaliates upon the organism by driving it to live at a faster pace than would be possible without it. This applies to every department of the process of vital existence. (Means)

Calorigenic Action.—The thyroid hormone directly increases the rate of oxidation of the tissue cells as measured directly in the calorimeter or indirectly by oxygen consumption (basal metabolic rate). The calorigenic *action of thyroid regulates heat production in homothermal animals*. In response to cold, increase in thyroid activity leads to increased heat production. The thyroid hormone functions as catalytic agent accelerating cellular metabolism. Other agents, such as epinephrine or dinitrophenol, perform similarly, but these lack the other important actions of the thyroid hormone.

Growth.—Athyroid animals are unable to attain adult form or function. In humans, congenital athyrosis results in cretinism, a form of dwarfism in which there is a marked retardation of physical and mental development.

During childhood, hypothyroidism produces an arrest of growth and development that may approach cretinism. In adults, hypothyroidism retards the growth of the skin which becomes dry, coarse and inelastic (myxedema). The hair becomes dry and brittle and grows very slowly. The beard in the male becomes scant. Due to retarded formation of red corpuscles, an anemia develops. Sterility, *amenorrhea and loss of sexual* activity are commonly encountered.

Metabolism of Food Stuffs.—The intermediary metabolism of carbohydrate, fat and protein is affected by the level of thyroid function. This is due partly to the calorigenic action of the hormone and partly to a direct action on other aspects of cellular metabolism. The hypothyroid individual has an increased sugar tolerance and an increased sensitivity to insulin. A large amount of protein is deposited in the body fluids. There is an increase in the blood fat (hypercholesterinemia) and body weight.

Thyroid feeding impairs the ability of the liver cells to store glycogen, diminishes insulin sensitivity, lowers the blood fat and produces a wasting of tissue protein (increased creatine excretion) so marked as to result in myasthenia and muscle atrophy.

Water Metabolism and Renal Function.—In hypothyroidism, along with the deposition of protein in the tissue spaces, there is a retention of water and salts. This is associated with a reduction in plasma volume, an increased viscosity of the serum and hyperproteinemia.

The administration of thyroid extract to hypothyroid and normal individuals alike causes diuresis. The hormone apparently has a direct renal action since it causes diuresis in the isolated kidney and produces an

intensification of the diuretic response to ingested water This action of thyroid has led to its use as a diuretic in nephrotic edema (p 706)

In myxedema the excess fluid comes from extracellular sources where it is found with 'deposit protein'

Central Nervous System—A normal level of thyroid activity is necessary for the functional integrity of both the central and autonomic nervous systems The athyroid individual may be intellectually retarded and emotionally shallow in contrast to the emotional lability, irritability and flight of ideas of the hyperthyroid

The activity of autonomic centers varies with the level of thyroid activity This association may be of importance in the pathogenesis of so called hyperthyroidism (p 1197) and may be the basis of epinephrine sensitivity in this condition

Endocrine System—The endocrine system as a whole is affected by the level of thyroid function There are alterations in the sensitivity to insulin The gonads are very susceptible to thyroid hypofunction The response to epinephrine is increased in thyrotoxicosis There is some evidence that the activity of the parathyroids parallels that of the thyroid gland

Iodine Metabolism—The thyroid gland is the chief regulator of iodine metabolism So far as is known the body uses iodine only in the manufacture of the thyroid hormone For this purpose about 0 2 mg is the daily requirement Excess of ingested iodine is excreted in the urine sweat saliva and bile

Pharmacology—Thyroid tissue contains thyroglobulin thyroxin and diiodotyrosine These three organic iodine compounds possess varying degrees of physiologic activity They are closely related to the true hormone

Thyroglobulin—Thyroglobulin is believed to be the form in which the hormone is stored in the colloid of the gland It is a complex protein of high molecular weight (675 000) it contains 7 7 per cent of iodine its *physiological activity is apparently equal to that of whole gland* Because of the large size of the molecule it is likely that thyroglobulin is converted into a simpler polypeptid on being released into the blood stream

Thyroxin—The alkaline hydrolysis of thyroglobulin yields *thyroxin* a crystalline product containing 65 per cent iodine It produces the same qualitative effects as *thyroglobulin* Thyroxin is a parahydroxyphenyl ester of tyrosine containing four iodine atoms It has been synthesized from two molecules of *diiodotyrosine*

Thyroxin crystallizes in sheaves and rosettes It is insoluble in most solvents Because of its two acidic groups (phenolic and carboxylic) it forms two series of salts The sodium salts are soluble in water

The physiological activity of thyroxin depends on its iodine content Removal of two iodine atoms yields *diiodothyronine* which is only one fortieth as active as thyroxin The removal of all the iodine yields *thyronine* which lacks activity An inactive compound is produced by elimination of the side chain of the thyroxin molecule

Diiodotyrosine—Thyroxin accounts for less than two thirds of the iodine present in thyroglobulin *The rest is present in diiodotyrosine* whose metabolic activity is only 1 10 000 that of thyroxin Although diiodoty

rosine loses its physiological potency when isolated in pure form or in the form of a polypeptide (diiodotyrosine peptone) it is as active as thyroxin in the thyroglobulin molecule

Diiodotyrosine peptone can be converted into an active protein containing thyroxin by the enzyme pepsin This suggests that through the action of enzymes diiodotyrosine is synthesized into the potent thyroid hormone in the body Since proteolytic digestion of thyroglobulin yields thyroxin and diiodotyrosine it is likely that both these molecules are linked through an amino acid to form thyroglobulin

Preparations —*Desiccated thyroid gland* and *thyroxin* are official preparations in the United States Pharmacopeia XII

Thyroid Extract U.S.P—Thyroid extract is described as the cleaned dried powdered thyroid gland deprived of connective tissue and fat and obtained from domesticated animals used for food by man It contains from 0 17 per cent to 0.23 per cent iodine in the form peculiar to the thyroid gland and is free of iodine in any other form The official average dose is one grain (60 mg) Tablets are marketed in the range of $\frac{1}{10}$ grain to 5 grains (6 to 300 mg)

Whenever possible thyroid extract should be administered after the basal metabolic rate has been estimated This may be compared with the resting pulse rate Once the relationship between B M.R and minute pulse rate has been established the latter may be used as a simple and inexpensive indicator of the former Thus if the original B M.R were —20 per cent with a resting pulse rate of 60 an elevation of the latter to the seventies would probably indicate that the basal rate approximated normal and a pulse rate in the eighties would suggest an elevation of the basal rate to above the normal figure approaching toxic manifestations

The estimation of optimum drug dosage is made difficult by the variations in subjective symptomatology Some patients with hypothyroidism feel best when their basal metabolic rates are approximately —10 per cent At higher levels although still in the minus zone they may complain of palpitation or tremor the latter being particularly annoying to professional and secretarial workers Other patients do not experience definite improvement until a B.M.R of 0 to +10 per cent is obtained

The calculation of the dosage of thyroid extract in hypothyroidism is divided into two components The *corrective dose* is the amount that is necessary to bring the patient to the normal level of basal metabolism Continuation of the corrective dose will naturally lead to hyperthyroidism It is necessary therefore to reduce the corrective dose to a *maintenance dose* This is most easily accomplished by continuing the usual daily dose and omitting the medication one or two days of the week Thus if the corrective dose is 2 grains daily the maintenance dose would be 2 grains daily except Saturday or Sunday or else 2 grains daily except Saturday and Sunday

Because of the protracted action of thyroid extract and the tendency to cumulation patients should be seen at least once weekly for several weeks until both the corrective and maintenance dosages have been satisfactorily worked out

Thyroxin U.S P—Thyroxin is the crystalline derivative of thyroglob-

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Iodine Metabolism—The thyroid gland is the chief regulator of iodine *metabolism* So far as is known the body *uses iodine only in the* manufacture of the thyroid hormone For this purpose about 0 2 mg is the daily requirement Excess of ingested iodine is excreted in the urine sweat saliva and bile

Pharmacology—Thyroid tissue contains thyroglobulin thyroxin and diiodotyrosine These three organic iodine compounds possess varying degrees of physiologic activity They are closely related to the true hormone

Thyroglobulin—Thyroglobulin is believed to be the form in which the hormone is stored in the colloid of the gland It is a complex protein of high molecular weight *(675 000)* it contains 7 7 per cent of *iodine its* physiological activity is apparently equal to that of whole gland Because of the large size of the molecule it is likely that thyroglobulin is converted into a simpler polypeptid on being released into the blood stream

Thyroxin—The alkaline hydrolysis of thyroglobulin yields *thyroxin* a crystalline product containing 65 per cent iodine It produces the same qualitative effects as *thyroglobulin* Thyroxin is a parahydroxyphenyl ester of tyrosine containing four iodine atoms It has been synthesized from two molecules of *diiodotyrosine*

Thyroxin crystallizes in sheaves and rosettes It is insoluble *in most* solvents Because of its two acidic groups (phenolic and carboxylic) it forms two series of salts The sodium salts are soluble in water

The physiological activity of thyroxin depends on its iodine content Removal of two iodine atoms yields *diiodothyronine* which is only one fortieth as active as thyroxin The removal of all the iodine yields *thyronine* which lacks activity An inactive compound is produced by elimination of the side chain of the thyroxin molecule

Diiodotyrosine—Thyroxin accounts for less than two thirds of the iodine present in thyroglobulin The rest *is present in diiodotyrosine* whose metabolic activity is only 1 10 000 that of thyroxin Although diiodoty

mation of thyrotropic hormone (p 1154) Excessive doses of thyroid extract tend to cause liver damage by impairing the deposition of glycogen

Physiological Disorders of the Thyroid

The functional disturbances of the thyroid include states of diminished and excessive secretion The hypothesis of an increased output of an altered molecule *hyperdysthyroidism* is not based on sound experimental or clinical observation Thyroid secretion is regulated by the anterior pituitary gland and perhaps also by the adrenal cortical hormone

HYPOTHYROIDISM

Deficiency of the thyroid secretion gives rise to hypothyroidism in which there is a generalized depression and retardation of all vital functions The clinical features are determined largely by the degree of glandular insufficiency and the age of the afflicted individual Congenital and postnatal hypothyroidism result in *cretinism* a form of imbecilic dwarfism Juvenile and adult *myxedema* are characterized by mental and physical deterioration a low basal metabolic rate a peculiar type of edema and regressive changes in the hair nails teeth and skin In each circumstance the fundamental disturbance is a diminished rate of cellular oxidation resulting from a primary lack of thyroid hormone which affects the life of the cell in every major aspect of its existence (Means)

CRETINISM

Congenital absence of the thyroid gland and its degeneration in early infancy give rise to a form of dwarfism known as cretinism Endemic cretinism occurs in regions where simple goiter is prevalent and the *sporadic* form is observed in nongoitrous regions anywhere in the world

Etiology—*Endemic cretinism* occurs in goiter regions" where the maternal iodine deficiency results in a more or less complete athyreosis It is rare in America but at one time was prevalent in Switzerland and Northern Italy *Sporadic cretinism* is more common in the female and is almost always due to congenital absence of the thyroid In rare instances the gland is destroyed by an acute infection or a congenital syphilis

Pathology—The cretinous thyroid gland may be absent, fibrotic or diffusely hyperplastic The brain is hypoplastic and there is a delay in the appearance of ossification centers and in epiphyseal union The gonads are atrophic but hypertrophy of the anterior pituitary and thymus are often noted

Clinical Manifestations—The clinical manifestations of cretinism usually appear during the second six months of life Occasionally the hypothyroid state is recognized as early as the third month and mild cases may go unnoticed for several years

At birth the child seems normal but tends to gain weight rapidly By the end of the first year the failure of normal growth and mental development attracts attention The child is late in sitting walking and talking Dentition is delayed and the anterior fontanelle remains open The characteristic facies is created by the widely spaced eyes the low forehead the broad based nose the thick eyelids and lips the half open mouth and the slightly protruding tongue The skin is rough and scaly and the hair dry and sparse The teeth appear late and decay early second dentition may

ulin It is marketed as a soluble *sodium salt* *Compressed oral tablets* are sold in dosages of 1 mg (1/60 grain) The pure crystals for intravenous use are sold in vials containing 10 mg

Thyroxin possesses no merit therapeutically for oral administration The tablets are considerably more expensive than those of the crude extract The soluble salts possess the advantage that they can be given parenterally, though the indications are exceedingly limited Occasionally a patient who is refractory to the oral administration of thyroid extract must receive the drug intravenously Intravenous thyroxin may also be employed as a desperation measure in the fulminating crises of thyrotoxicosis

In comparing the relative efficiency of crude thyroid extract and pure thyroxin it should be realized that 1/80 grain of the latter approximates the action of 3 to 5 grains of the former

The oral tablets of thyroxin are often so hard that unless they are fragmented before swallowing they may pass in the stool The patient should be instructed to crush the tablet between the teeth or grind it in a mortar or between spoons

Assay—The physiologic potency of thyroid preparations may be determined quantitatively by several methods These include the measurement of the rate of gaseous metabolism of normal guinea pigs the study of the action on amphibian metamorphosis and the determination of the protective action of thyroid against the toxic effects of acetonitrile in mice (Reid Hunt)

The commercial preparations of thyroid need not be assayed since their activity is proportional to their organic iodine content Thyroxin being a compound of definite composition, is dispensed by weight

Absorption Excretion Duration of Action—The absorption of thyroid extract and thyroxin from the intestine is variable The effect of a single dose of either compound appears in twenty four hours and reaches a peak in from five to ten days After the administration of the hormone has been stopped seventy to eighty days may elapse before the metabolic rate returns to normal As already mentioned in determining the level of dosage the importance of cumulative action should be considered

Therapeutics—Specific therapeutic effects of thyroid extract are observed in the treatment of *cretinism* (p 1191), *juvenile myxedema* (p 1193) and *adult myxedema* (p 1193) Nonspecific beneficial activities are noted in non myxedematous patients with low basal metabolic rate and in obesity (p 695), sterility (p 2418) habitual abortion (p 2653) the nephrotic syndrome (p 2389) and a variety of miscellaneous conditions such as dermatoses characterized by dryness of the skin and induration

The Effects of Thyroid Overdosage—Excessive doses of thyroid extract produce many of the phenomena of thyrotoxicosis the increase in basal metabolic rate tachycardia irritability weight loss tremor increase in appetite and diarrhea However exophthalmos does not occur (See *Pathogenesis of Graves Disease*)

Large doses of thyroid extract produce a decrease in endogenous thyroid function in normal and in hyperthyroid patients In normal patients this may cause the onset of myxedema after thyroid is stopped The effect may be mediated through the anterior pituitary by suppressing the for

of normal growth Mental development usually remains retarded because *of irreversible damage to the central nervous system*

JUVENILE MYXEDEMA

The occurrence of hypothyroidism in childhood gives rise to a syndrome intermediate between *cretinism* and *myxedema* The condition is rare and the etiologic factors are largely unknown In a few instances the disease has followed an acute infectious disease of childhood

The principal symptoms are similar to those of cretinism and myxedema The child is noticed to have lost abilities previously acquired and becomes asocial The degree of skeletal retardation is dependent on the age of onset and the severity of the disease and varies from extreme dwarfism to a slight stunting of normal growth Early diagnosis and the prompt institution of therapy may be attended by satisfactory improvement

MYXEDEMA

Adult hypothyroidism was described by Gull (1873) as a cretinoid condition occurring in women Four years later Ord (1877) associated it with atrophy of the thyroid and introduced the term *myxedema* because of the appearance of the skin Subsequently it was shown that a similar condition followed surgical removal of the human thyroid (*cachexia strumipriva*) The first instance of successful replacement therapy for endocrine hypofunction in man was the use of thyroid extract by Murray (1891) for the control of myxedema

Etiology—Myxedema occurs spontaneously or it may follow operative removal of the thyroid gland The spontaneous variety is rare in its severe form but mild manifestations occur more commonly than is generally recognized The factors responsible for the decrease in thyroid activity usually are unknown and the condition is then ascribed to a *primary atrophy* Anterior pituitary insufficiency may give rise to a clinical state resembling myxedema and in some instances the syndrome is the late result of *acute* or *chronic thyroiditis* *endemic goiter* or *hyperthyroidism*

Postoperative myxedema follows surgical removal of the thyroid gland for hyperthyroidism malignancy or simple adenoma It may appear within a few weeks months or even years after thyroidectomy In recent years *surgical myxedema* has been induced therapeutically in the treatment of *chronic congestive heart failure severe coronary artery disease* with *status anginosus* and *chronic lymphatic leukemia*

Pathology—The thyroid gland of myxedema is small and fibrotic Microscopically there is a marked decrease in the epithelial cells an increase in connective tissue and considerable infiltration with small round lymphocytic cells The tissues of the body are affected by a *mucinous infiltration* best seen in the subcutaneous tissues of the face supraclavicular regions and neck and in the mucous membranes of the mouth vagina and anus The peritoneum is pale and thickened so that its appearance suggests a chronic inflammatory induration The joints and ligaments are thickened and infiltrated the heart is enlarged and the pericardium is thickened and may be distended by fluid The myocardium shows few microscopic changes

The edema fluid is believed related to other mucinous tissues such as Wharton's jelly It has a high protein content

Clinical Manifestations—The onset of spontaneous myxedema is slow and insidious Women are more commonly affected than men (in the ratio of 5 to 1) and the symptoms are usually first noted in the fifth decade In many patients a colloid goiter or a simple adenoma has been present for many years In a few instances the condition is the end phase

be delayed until adult life The neck is short and thick and the abdomen is large and pendulous An umbilical hernia is usually present

As the years pass the general retardation becomes more apparent and the body is greatly dwarfed At the age of fifteen the individual may be only 2 or 3 feet tall The extremities are short in relation to the trunk the distance from the umbilicus to the sole is less than that from the umbilicus to the top of the head Fatty deposits about the size of a hen s egg are seen in the supraclavicular regions The voice is hoarse and rough, the gait is waddling and clumsy The temperature is often subnormal and may remain so during an acute infection There is marked mental impairment and imbecility is common The vocabulary is limited and speech may be impossible Even untreated cretins may however live to an advanced age

Laboratory Data —When cretinism is suspected a number of laboratory aids are of diagnostic value *Roentgen examination* of the skeleton shows a delay in the appearance of the nuclei of the carpal and tarsal bones and the epiphyses of the long bones remain ununited well beyond the twentieth year *Serum cholesterol* is increased and values of 400–500 mg per



Fig 250 —Cretin Note large size of tongue *

cent are commonly encountered The *basal metabolic rate* is subnormal but often cannot be performed satisfactorily through inability of the patient to cooperate

Treatment —The response to replacement therapy with thyroid extract is less favorable in cretinism than in the other varieties of hypothyroidism The success of therapy is enhanced by early recognition of the disease and the early administration of adequate doses of *thyroid* If cretinism is recognized before the age of six months favorable result may be anticipated Cretins of five to ten years may be helped if the condition is mild but older cretins are often made uncomfortable by thyroid therapy

The *thyroid ration* in cretinism must be close to the maximum nontoxic dose The following dosages of U S P thyroid extract are suggested by Means at two to four months $1/10$ grain per day four to eight months $1/5$ grain per day eight to twelve months $3/10$ grain per day twelve to twenty four months $2/5$ to $3/4$ grain per day two to four years $1/2$ to $1\frac{1}{2}$ grains per day four to twelve years 1 to 3 grains daily The criteria of adequate dosage are a normal basal metabolic rate and the maintenance

* Major Physical Diagnosis

Physical Examination —The general appearance of fully developed myx edema is fairly typical The face is expressionless and has been termed stupid and bovine, the features are coarse and may suggest an acromeg aly The eyelids are heavy and markedly puffed so that palpebral fissures are reduced to narrow slits the nose is thick the lips protrude and the cheeks are flabby forming heavy jowls The tongue is greatly enlarged and heavily coated and speech is clumsy and thick The hairs of the head eyelashes and eyebrows are scant dry and lusterless A suggestive sign of myxedema is the absence of the outer third of the eyebrows The skin of the face has a lemon yellow pallor which tends to accentuate a not uncommon malar flush Conjunctivae and oral mucosae are pale

The general habitus is heavy and ponderous The fingers are short stubby and thick the hand may have a *spade like* appearance there are *localized fat pads* in the supraclavicular regions over the hips and over the anterior surface of the lower abdomen forming a definite panniculus there is frequently a well developed *dorsal kyphosis* which is accentuated by a cervical fat pad

The *skin* of the extremities and body is dry rough inelastic and cold the *subcutaneous tissues* are thick and swollen but do not pit on pressure The *nails* are thick ridged and easily broken There is little hair in the axilla or pubic regions or on the male chest legs and beard areas the growth of hair and nails is slow Cutaneous injuries heal slowly scaly eczematoid and ichthyotic eruptions are common and there is an almost complete absence of sweating

The *tongue* is thick and coated it is often too large for the oral cavity The vocal cords are lax and thickened and these changes are largely re sponsible for the *clumsy speech* the difficulty in enunciation and the deep husky voice The articular ligaments often are lax and the joints are easily hyperextended Movements are slow and the tendon reflexes are de pressed Numbness and tingling in the extremities are frequent and all sensory modalities are diminished

The *heart* is enlarged and the sounds are feeble the pulse is small slow and weak the cardiac enlargement usually is due to myocardial weakness leading to dilatation There may be a pericardial effusion Flu oroscopically the cardiac contractions are sluggish and of small amplitude Cardiac failure is rare The *blood pressure* is usually low but there may be marked hypertension cardiac hypertrophy granular kidneys and se vere arteriosclerosis The hypertension may subside after treatment with thyroid

Laboratory Data —The *basal metabolic rate* is subnormal the degree of depression roughly paralleling the severity of the clinical condition Usu ally the reading approximates —30 per cent but there is a range of vari ation between —10 and —45 per cent The clinical picture of myxedema is not due to the hypometabolism since lowered rates exist from other causes in the absence of the features of hypothyroidism In postoperative hypothyroidism the fall of the basal metabolic rate precedes by several months the appearance of the clinical features

See *Differential Diagnosis of Decreased Basal Metabolic Rate* (p 719)

The fasting *blood sugar* is frequently below normal and glucose tol erance is increased after oral and intravenous tests Frank hypoglycemic

of hyperthyroidism that has "burned out" and it may follow a thyroid operation or the prolonged administration of thyroid extract to normal subjects

The myxedematous patient discloses a *general depression* of mental activity changes in personality and intellect weakness sensitivity to cold and dyspnea The mind is dulled memory is poor judgment is lost and there is a lack of initiative In contrast to the vivacity and continual flight of ideas of the hyperthyroid individual the myxedematous patient is usually placid emotionless apathetic and disinterested Occasionally the patient is extremely irritable easily excited and may present the features of a major psychosis

The lowering of the basal heat production gives rise to a *sensitivity to cold* and the preference for a warm environment There is a sensation of



A



B

Fig 251—Twenty six year-old woman with myxedema *A* Before treatment Basal metabolic rate —36 *B* Same patient two months later after treatment with desiccated thyroid gland Basal metabolic rate —5 *

chilliness when the external temperature causes no discomfort to normal individuals Perspiration is decreased and the skin is dry rough and cold The decreased catabolism favors a moderate increase in *body weight* *Dyspnea* is common on exertion or at rest there may be episodes of precordial oppression *Fatigue* is constant and may be so pronounced that normal physical activity is impossible Movements are slow and clumsy and it may be impossible to perform skilled acts The gait may be ataxic

See *Differential Diagnosis of Gain in Weight* (p 700)

Miscellaneous symptoms include anorexia marked constipation and depression of the special senses leading to deafness anosmia and loss of visual acuity In women before the menopause the principal symptom may be *menorrhagia* Repeated abortions are common and may be the only indication of a moderate decrease in thyroid activity

* DuBois in Cecil Textbook of Medicine

ment therapy in the various clinical forms of hypothyroidism The curative treatment of adult myxedema is as perfect a form of therapy as any known to medicine Patients with myxedema have been maintained in a normal condition for more than twenty years by the daily use of a maintenance dose of thyroid Treatment aims to rid the patient of symptoms with the smallest possible dose of thyroid and should not be determined by any preconceived notion of the normal basal metabolic rate

The simplest and the best method of treatment is the use of tablets of *desiccated thyroid* by mouth It is advisable to start with a minute dose 16 mg (¼ grain) of thyroid and then gradually increase the dose over a period of weeks until the smallest dose producing complete symptomatic relief is determined This constitutes the daily dose of thyroid necessary during the remainder of the patient s life Many patients prefer to take thyroid in the morning since it gives them increased vitality during the day while an evening dose may cause sleeplessness It is important to accustom the patient to the use of one commercial brand of thyroid in view of the variation in iodine content and potency of the several available preparations Most patients are relieved by a dose of USP thyroid lying between 1½ and 3 grains

The response of the myxedematous patient to thyroid is prompt and striking One of the first changes is a diuresis with a loss of weight which occurs within the first two or three days There is a liberation of water and electrolyte stored in the tissue spaces as the deposit protein is oxidized The expression of the face returns to normal and the puffy appearance is lost but the coarseness and scaliness of the skin take longer to regress Within a week the basal metabolic rate may approach normal levels and there is an increase in spontaneity and reactivity Bowel action becomes more free and normal sexual function is restored

It is important to guard against untoward effects when giving thyroid to patients with myxedema An excessive dose may result in cardiac pain heart failure muscle pain and cramps in the extremities Under these circumstances the drug is stopped until the symptoms disappear and then resumed in a smaller dose

HYPERTHYROIDISM

The term hyperthyroidism is employed for convenience throughout this discussion to embrace the clinical states variously termed *Graves syndrome Basedow s disease exophthalmic goiter toxic adenoma* and *adenomatous goiter with hyperfunction* The multiple terminology suggests the uncertain state of our knowledge Historically the captions lack accuracy since the earliest satisfactory description was that of Caleb Parry of Bath (1786) Clinically and physiologically the implications of the nomenclature are even more disturbing Exophthalmic goiter may be present without exophthalmos or goiter toxic adenoma implies a metabolic abnormality whose existence is doubtful

Clinical hyperthyroidism is commonly delineated by cataloguing the major symptoms of tachycardia tremor exophthalmos and goiter together with the minor manifestations which include nervousness sweating asthenia and diarrhea To these clinical manifestations has been added the laboratory evidence of elevation of the basal metabolic rate The relation

episodes are uncommon In some cases of severe diabetes mellitus total thyroidectomy has been accompanied by amelioration of the abnormality of carbohydrate metabolism The total *blood lipids* are increased and the *blood cholesterol* may rise to 500 or 600 mg per cent The degree of hyperlipemia and hypercholesteremia parallels the depression of the basal metabolic rate and is perhaps a more constant index of hypothyroidism The increase in *plasma carotene* is responsible for the yellowish discoloration of the skin

The *blood iodine* is low and in severe deficiency the organic fraction may be entirely absent There is a *diminished iodine tolerance* as indicated by the sharp rise in blood iodine and its rapid urinary excretion after oral administration

A moderate *anemia* is present in many patients while the white blood cells and platelets are normal The anemia is frequently associated with *achlorhydria* and the clinical picture may closely resemble a *hyperchromic anemia* and respond to the administration of liver extract before the basal metabolism rises in response to thyroid The anemia is usually due to a combination of thyroid deficiency which inhibits the normal activity of the bone marrow achlorhydria a dietary deficiency with respect to iron and chronic blood loss from the menorrhagia that often precedes the menopause

The *urine* is usually normal in amount and commonly contains albumin and formed elements There is no obvious impairment of renal function Following the administration of thyroid there is a transient diuresis In untreated cases the urine contains an excess of *thyrotropic hormone* The urinary excretions of iodine calcium and creatine are decreased

The characteristic *electrocardiogram* shows low voltage in all leads The P R intervals may be prolonged and there may be changes in the QRS complex the R T interval and the direction of the T wave Partial and complete heart block are encountered The electrocardiographic abnormalities regress promptly after the administration of thyroid

Course —Myxedema is slowly progressive and death is usually due to an intercurrent acute infection pulmonary tuberculosis or a cardiovascular complication such as coronary occlusion or congestive heart failure Some patients develop a terminal cachexia culminating in coma In the *spontaneous variety recovery may occur if sufficient hyperplasia* of the remaining thyroid tissue takes place In postoperative myxedema the hypothyroid state may be transient and eventually regresses as the thyroid remnant becomes functionally adequate

Diagnosis —The recognition of fully developed myxedema is simple in the presence of a low basal metabolic rate and a fairly typical clinical *picture* In the presence of a moderate or severe anemia the condition may closely resemble *macrocytic hyperchromic anemia* *Chronic nephritis* may require careful differentiation Myxedema may be confused with a mild *acromegaly* but careful study quickly reveals the correct diagnosis In rare cases of *localized amyloidosis* (Lubarsch Pick syndrome) the enlarged tongue (due to amyloid deposits) may suggest myxedema The response to therapy is so specific as to constitute a pathognomonic test

See *Differential Diagnosis of Gain in Weight* (p 695)

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ship of these diverse phenomena may be clarified by a consideration of the physiology of the thyroid its related glands and the involuntary nervous system

Pathogenesis —*The parenchymal cells of the thyroid gland abstract iodine* and *tryptophan* from the circulating fluids and manufacture *thyroxin* a specific iodide-containing hormone and a *colloid substance* in which the iodine or thyroxin is stored Thyroxin probably leaves the gland through both lymphatics and veins Since the concentration of thyroxin in the blood of human patients cannot be measured the demonstration of the hyperthyroid state is dependent upon presumptive evidence which is histologic pharmocologic and chemical

Hyperplasia and Hyperfunction —Histologic inferences concerning the hyperthyroid state are based on the hyperplasia of the gland that is commonly but not invariably observed Hyperplasia of the gland is not limited to hyperthyroidism It may occur in *simple* or *endemic goiter* or human *cretinism* The histological picture is independent of thyroid function *but is determined by iodine storage* a decreased concentration *of the element giving* rise to hyperplasia The tenet that hyperplasia indicates hypersecretion is not in accord with fact

Thyroid Feeding —Indirect pharmacologic evidence of the presence of hyperthyroidism has been suggested through the resemblance of the clinical syndrome to the symptoms produced artificially by the ingestion of thyroid extract or the injection of crystalline thyroxin Unfortunately the pharmacologic resemblance to clinical hyperthyroidism is imperfect Carlson after extensive studies of thyroid feeding stated It would require considerable imagination or an undue influence of one s wish or one s judgment to identify the symptom-complex of excessive thyroid feeding in experimental animals with exophthalmic goiter" Every clinician has known many patients who have taken thyroid extract over long periods of time *in order to effect weight reduction These patients manifest transitory symptoms* as the result of overdosage with the drug The symptoms abate when the drug has been discontinued and excreted If true hyperthyroidism develops it is a rare experience and more likely coincidental than of causal relationship Exophthalmos is a prominent feature of clinical hyperthyroidism yet it cannot be produced by thyroid feeding it is frequently not ameliorated significantly by thyroidectomy and may even progress in the face of an operative procedure sufficient to cause myxedema Poisoning with thyroid extract is not identical with clinical hyperthyroidism though the two conditions have much in common

Iodine Metabolism —Indirect chemical inferences pertaining to hyperthyroidism have been suggested by studies of iodine metabolism *Low iodine figures* in the blood are consistently found in endemic goiter In clinical hyperthyroidism both high and normal quantities have been described the latter particularly in patients whose disease has existed for more than a year Failure to demonstrate a consistently increased blood iodine may not necessarily argue against the possibility of hyperthyroidism It indicates merely that the ratio of manufacture to destruction or excretion of the hormone does not consistently lead to increased blood concentration Curtis and Philips studied the entire iodine economy in patients with hyperthyroidism They demonstrated a negative balance due to excessive loss of iodine in urine *blood sweat and stool and suggested that there is a true iodine diabetes* in hyperthyroidism Even this important and interesting work leaves much to be desired of indirect evidence that hyperthyroidism exists If *hyperiodemia* suggests hyperthyroidism what is the explanation of the relief of symptoms attendant upon iodine therapy? Surely if increased blood iodine indicates hyperthyroidism an added supply of the element should augment rather than ameliorate symptoms

Toxic Adenomas —The state of confusion concerning hyperthyroidism has been increased by theories concerning the toxicity of adenomas The known facts concerning thyroid adenomas may be briefly summarized Interpolated in the thyroid tissue as in all other parenchymal tissue there are frequently observed isolated and encapsulated rests or adenomas These function less actively than the nontumor tissue of the surrounding gland hence they *cannot of themselves*, independently hypersecrete or give rise to clinical symptomatology except to participate in a process initiated and perpetuated by the surrounding nontumor tissue They may be present in cretinism endemic goiter normal glands or in hyperthyroidism Hypotheses suggesting toxicity of adenomas and the existence of hyperdysthyroidism not only lack positive proof but there is much tangible evidence to refute their accuracy

Effects of Thyroidectomy—Though laboratory evidence is lacking for proof of the hyperthyroid state it is a clinical fact that *subtotal thyroidectomy relieves most of the distress g symptoms* of patients suffering from clinical hyperthyroidism There is much to suggest that the role of the thyroid may be intermediary The amelioration of symptoms following thyroidectomy may be due to a decrease in the production capacity of the thyroid gland and the severance of a link in the chain of disturbed physiological mechanism initiating in the midbrain or the anterior pituitary gland If the role of the thyroid gland be of secondary importance in clinical hyperthyroidism the aim of specific therapeutic procedure would be directed toward the correction of the more fundamental disturbance In consequence the possible participation of factors other than the thyroid gland warrants scrutiny These factors may be sought in internal secretory glands other than the thyroid in the involuntary nervous system or in a psychosomatic mechanism of basic biologic significance

Participation of Other Endocrine Glands—There are many clinical observations that suggest in hyperthyroidism a primary disturbance of internal secretory glands other than the thyroid with secondary thyroid participation Halsted was so impressed with the *thymic enlargement* in hyperthyroidism that he advocated and performed thymectomy Clinically there are many interesting interrelationships between thyroid and *ovary* Women greatly outnumber men in the incidence of hyperthyroidism Since amenorrhea is a frequent symptom of the disturbance the various ovarian extracts have been employed therapeutically but without consistently successful results

An interrelationship of thyroid and *adrenal medulla* was suggested by the work of Cannon and his collaborators Attempts were made to prove the existence of an increased output of epinephrine or a sensitization of the involuntary nervous system to the action of the epinephrine through synergism with thyroxin These experiments though they could not be confirmed induced Crile to approach the surgical therapy of clinical hyperthyroidism by denervation of the adrenal medulla or partial removal of its substance a practice not generally accepted and now abandoned

Marine demonstrated an interrelationship between *adrenal cortex* and thyroid Destruction or freezing of cortex led to elevation of the basal metabolic rate and simulation in laboratory animals of clinical hyperthyroidism Extracts of adrenal cortex have been tried therapeutically but to no great avail

More recently Collip and others isolated a thyrotropic substance in the *anterior pituitary gland* Occasionally a suggestion of the clinical interrelationship is seen in the association of acromegaly and hyperthyroidism The thyrotropic hormone may produce in laboratory animals a syndrome simulating clinical hyperthyroidism with exophthalmos The *sella turcica* has been irradiated in the attempt to treat hyperthyroidism by reduction or inhibition of the thyrotropic hormone but this has yielded no clinical success Because of the presumptive inhibition of the gonadotropic factor of the *pituitary gland* by the male sex hormone testosterone has been employed in an attempt to inhibit the thyrotropic factor but the results thus far have not been encouraging

The present status of the interrelationship of thyroid and other internal secretory glands may be summarized briefly Many important interplays are demonstrable These relationships are interesting and suggestive but therapeutically unfruitful However these physiological approaches to the elucidation of the mechanism of hyperthyroidism indicate a mechanism beyond the thyroid gland and suggest that one day our present forms of therapy may be rendered archaic by the discovery for the control of the disturbance of some specific physiological or pharmacological agent

The Role of the Involuntary Nervous System—The presenting symptoms in clinical hyperthyroidism are *sympathomimetic* and may be produced by emotional or chemical stimulation of the adrenergic portion of the involuntary nervous system Whatever may be the ultimate agency producing hyperthyroidism there is no doubt but that eventually the causative mechanism operates through the intervention of the involuntary nervous system With the exception of epinephrine the principles derived from the ductless glands are not sympathomimetic Were a state of hyperepinephrinemia demonstrable the problem of hyperthyroidism might be considerably simplified but this state does not and cannot exist as shown by the assays performed by Stewart and Rogoff of the blood of the inferior vena cava pocket The fascinating and suggestive hypothesis of emergency hyperepinephrinemia fails of physiological proof but the specific diminution of organically bound magnesium in hyperthyroidism may have important significance

Autonomic Imbalance—If physiologic and pharmacologic methods have failed to elucidate the role of the involuntary nervous system in hyperthyroidism many clinical observations are suggestive Virtually all patients who develop hyperthyroidism give a history of a pre-existent instability of the involuntary nervous system This autonomic imbalance is usually the precursor or diathesis on which hyperthyroidism is superimposed when a metabolic disturbance characterized by increased catabolism supervenes When the metabolic state is restored to normalcy the patient reverts to autonomic imbalance and the residual symptoms following the relief of hyperthyroidism are identical with the early symptoms of the constitutional autonomic imbalance (p 1395)

Hyperthyroidism is seen occasionally in association with organic disease of the nervous system The disease may occur rapidly after an acute encephalitis when it is associated with evidences of hypothalamic injury such as Parkinsonism This observation suggests an inhibitory influence of the diencephalon over thyroid function

Patients with autonomic imbalance present psychic and emotional instability and a bewildering variety of functional disturbances in organs which show no evidence of organic change The catalogue of symptoms and signs in autonomic imbalance includes vasomotor instability manifested by cold hands and feet with or without excessive sweating flushing blushing and blanching urticaria and other neurodermatides lability of the pulse rate and blood pressure disturbances in motility and tonicity of smooth muscle and secretory alterations in glandular structures Though the manifestations of autonomic imbalance may be legion each patient presents an individual reaction picture evoked by emotion fatigue or the introduction of specific drugs There is no significant elevation of the basal metabolic rate The thyroid gland may be normal There are no positive laboratory findings that are pertinent to the symptomatology There may be present the alterations in the adrenalin sensitivity and the creatine metabolism believed respectively by Goetsch and Shorr to be specific for hyperthyroidism

The concept of autonomic imbalance is essential to the understanding of the problem of hyperthyroidism Inherent in the discussion of the mechanism of hyperthyroidism is the consideration of the factors that regulate the tonicity of the involuntary nervous system The knowledge of either one of these problems will go far to the solution of the other Since thyroxin is not sympathomimetic and there is no proof that sympathomimetic activity can give rise directly or indirectly to significant augmentation of thyroxin effect the mechanism by which these agencies participate in the production of hyperthyroidism remains obscure

Biological Factors—If the mechanism of hyperthyroidism cannot be fully explained by humoral or neurogenic factors it may not be amiss to inquire into broader implications Biologically speaking thyroxin is not essential to life Phylogenetically the gland is first observed in amphibians where its function is characterized by (1) Accelerating metamorphosis in species that normally undergo this change or (2) actually producing metamorphosis in certain salamanders which in nature undergo no metamorphosis These changes have led Uhlenhuth to state They demonstrate at what a phylogenetic stage the amphibians and perhaps the entire higher vertebrates would be if they had not developed the thyroid mechanism In the higher vertebrates the main and perhaps the sole function of thyroxin is as a catalyst accelerating most if not all biologic and metabolic processes Whether or not thyroxin contributes new functions is an academic point which need not concern us at this time The phylogenetic appearance of the thyroid gland at the amphibian level and its catalytic function in the human economy are of profound significance in discussions of the etiology and pathogenesis of hyperthyroidism To the best of our knowledge hyperthyroidism occurs spontaneously only in man and perhaps only in civilized man McCarrison for example never observed hyperthyroidism in the native Indian until Indian troops were sent to the First World War

There is presumptive evidence that hyperthyroidism may be a disturbance of historically recent origin and that its incidence is rapidly increasing The clinical appearance of the patient with *hyperthyroidism is dramatic easily recognizable and unforgettable* Though endemic goiter was known to the Egyptian and Grecian physicians and the painters of primitives the first medical description of hyperthyroidism appeared in 1802 The four pioneers who described cases between 1802 and 1840 Flajani in Italy Parry who practiced in Bath from 1780 to 1816 Graves of Dublin and von Basedow of Merseburg reported a total of but fifteen patients Certainly a practitioner today comparable to Parry practicing in Bath for thirty six years sees more than five cases of hyperthyroidism Could Parry once recognizing hyperthyroidism have missed other cases that occurred in his practice or was the disease so rare that he saw on the average but one case every seven years? The specu

lation is not idle for if hyperthyroidism is a condition of recent origin and vastly increased incidence occurring *only or almost exclusively in civilized man the psychic component in its* etiology and pathogenesis assumes greater importance The explanation of our inability to *observe or produce the syndrome in its entirety in experimental animals or to comprehend* its mechanism in the clinic may rest on these biological and psychological grounds

Summary—It is apparent that the etiology and pathogenesis of hyperthyroidism are still to be elucidated Means in his recent and excellent treatise on the thyroid gland and its disorders writes "Since in the majority of cases of exophthalmic goiter no etiologic agent or likely causative factor thus far has been found and since the disease has not been perfectly reproduced in experimental animals it must be admitted freely that in contrast to endemic goiter the cause of the disease remains quite unknown Hoover averred There is certainly no evidence of superfunction of the thyroid gland All the evidence seems to indicate that hyperplasia, so called is evidence of incompetence of the gland and *is associated* with hypofunction rather than hyperfunction"

Present knowledge of clinical hyperthyroidism is summarized by the statement that it is a complicated syndrome consisting of neurogenic metabolic and glandular components There are present (1) a diminished storage of iodine in the thyroid gland giving rise to hyperplasia, (2) a collection of sympathomimetic symptoms and (3) a general increase in the catabolic processes the latter alleviated temporarily by iodine therapy and more lastingly by thyroidectomy No one of the components of clinical hyperthyroidism is pathognomonic Increase in the catabolic process may occur in conditions unassociated with disturbances in the thyroid gland or the involuntary nervous system Sympathomimetic manifestations may be present with or without alterations in the thyroid gland or the basal metabolic rate Thyroid hyperplasia may occur in otherwise normal individuals and in patients with an elevated or diminished basal metabolic rate

The complete clinical picture of hyperthyroidism consists in the simultaneous presence of the three abnormalities The autonomic imbalance precedes and is the precursor of hyperthyroidism When the catabolic phenomena are superimposed the clinical picture of hyperthyroidism is complete When the catabolic process has abated the autonomic imbalance persists and somehow somewhere in the pathogenesis of this process there enters the exciting factor of a psychosomatic relationship that seems to be related to the phylogenetic approach to what we call civilization

Pathology—*The introduction of iodide therapy* in the management of hyperthyroidism has resulted in the rare appearance of the unmodified pathological picture in the thyroid *gland*

Pre iodide Hyperplasia—In the pre iodide era the classical appearance was that of a *diffuse enlargement engorgement* and *hyperplasia* The *lining cells of the thyroid follicles* were increased in size and their numbers were so augmented that the necessary infoldings practically eliminated the lumen and no colloid material was demonstrable The vessels were dilated and engorged In long standing examples the arterial walls were considerably thickened and cystic areas were observed The vascularity was so extreme that the gland seemed almost to function as an *arteriovenous shunt*

Adenomas—The thyroid changes are usually uniform but occasionally one lobe appears *larger than the other* Scattered throughout the tissues are variable numbers of adenomas and these share in the pathologic disturbances that are better noted in the nontumor tissue of the gland At times these adenomas are so extensive that *they appear to dominate* the pathologic picture leading to the concept that they are toxic and suggesting that the remaining thyroid tissue participates inconsequentially in the clinical disturbance Against this concept is the fact that the administration of iodine causes a prior change in the non adenomatous thyroid portion suggesting that it functions more actively than the adenoma Furthermore removal of the adenoma without significantly reducing the bulk of the non tumorous gland fails to alleviate the clinical syndrome

Iodized Thyroid—*The administration of iodine* alters the appearance of the thyroid tissue The hyperplasia tends to abate there is a *reversion to the colloid phase* On rare occasions the appearance of the gland approaches normal The lack of *specificity in thyroid* pathology is emphasized by the appearance of an indistinguishable hyperplasia in the non toxic goiter of iodine deficiency and in occasional instances of cretinism The iodine content of the hyperplastic gland is significantly decreased in any event, suggesting that the relationship between morphology and function has to do with storage rather than secretory activity

Changes Other Than Thyroidal—In addition to the changes in the thyroid gland pa-

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tients who constitute the group of masked hyperthyroids often with cardiac invalidism

A progressive *loss in weight* occurs despite an unusually large caloric intake The weight loss may precede the recognition of the other manifestations of the disease and varies with the degree of elevation of the basal metabolic rate Occasionally the state of nutrition is maintained through hyperalimentation but in severe instances more than one fifth of the body weight may be lost within a few weeks The loss in weight is due to the increased catabolism the presence of disturbed gastro intestinal functions and alterations in the metabolism of carbohydrate fat and protein See *Differential Diagnosis of Loss of Weight* (p 700)

Fatigue and *asthenia* are pronounced and may be sufficiently severe to keep the patient in bed There is obvious weakness of the voluntary musculature first observed by the difficulty in climbing stairs Extreme muscle fatigue may suggest a myasthenia gravis but the therapeutic test with physostigmine (p 2886) clarifies this difficulty Loss of *muscle volume* is so extreme as to simulate a malignant cachexia

Palpitation is a frequent complaint and is often a troublesome cause of insomnia It is usually associated with moderate or severe *tachycardia* but may occur in the presence of a mild increase in pulse rate The palpitation may be paroxysmal and associated with *precordial oppression* and *dyspnea* as a result of transient *auricular fibrillation*

The increased production of heat produces a train of characteristic phenomena There is a distinct preference for cold and distaste for hot weather Profuse *perspiration* occurs at rest and after slight exertion Night sweats occur as in tuberculosis The constant sweating frequently leads to *pruritus* which may be generalized

Diarrhea is a frequent and early symptom It is usually periodic and unaccompanied by evidences of acute enteritis It is refractory to the usual methods of treatment and often is associated with achlorhydria

Physical Examination —The general appearance of the hyperthyroid patient is so characteristic that the diagnosis often is established at a glance The usual subject is a young female with wide staring eyes an appearance of marked anxiety or fear a warm flushed skin which is being constantly mopped and an obvious increase in psychomotor activity The characteristic facial expression is due to the tendency to protrusion of the globe which gives rise to the distinctive eye signs In addition to the stare and the glazed appearance of the cornea is the failure of the upper lid to follow the eyeball on looking downward (Von Graefe s sign) the *palpebral fissure* is widened leaving an area of exposed sclera above the cornea (*Dalrymple s sign*) and blinking is infrequent and incomplete (*Stellwag s sign*) The last phenomena are attributed to spasm of the levator palpebrae superioris In addition the ability to converge is impaired (*Mobius sign*) fatigue of the eye muscles is common (*asthenopia*) and some patients reveal a partial or complete external *ophthalmoplegia*

Exophthalmos —Exophthalmos is present in most patients It is usually symmetrical but may be more marked on one side or completely unilateral Its occurrence is more frequent in patients who develop the disease before rather than after the thirty fifth year Paradoxically it may progress after the thyrotoxicosis has been completely eliminated by subtotal

tients with hyperthyroidism show more distant and widespread pathologic variations In about 50 to 60 per cent of the patients there is a persistent and enlarged *thymus* a generalized hyperplasia of *lymphoid tissue* and palpable enlargements of the *spleen* and *lymph nodes* The heart is usually unchanged but there may be evidences of *myocardial damage* particularly *fatty degeneration* Patients who have died of an acute thyrotoxic crisis reveal degenerative changes in the *liver* the *skeletal muscles* are often atrophic and wasted with considerably fatty infiltration These changes are especially marked in the external ocular muscles *Exophthalmos* produces considerable edema and an increase in fat in the retrobulbar space

Clinical Manifestations—Hyperthyroidism is more common in the *female* occurring in the proportion of ten females to one male It is essentially a disease of adolescence and young adults but occurs at all ages It is rare in infancy and old age and is decidedly less common in aborigines if it occurs at all in primitives Its occurrence is usually associated with the attainment of a relatively high social and educational level This feature has led to the belief that in the pathogenesis of hyperthyroidism 'there enters the exciting factor of a psychosomatic relationship that seems to be related to the phylogenetic approach to what we call civilization Although the onset of the disturbance may be abrupt without antecedent manifestations more often there is a prolonged history of *autonomic imbalance*, a secondary phase of the superimposition of a *precipitating factor* and a gradual and insidious onset of the symptoms of *hyperthyroidism* developing almost imperceptibly over periods of weeks or months

The Pre existent Autonomic Imbalance—The clinical symptomatology of autonomic imbalance is elsewhere detailed (p 1395) The vast majority of patients who later develop hyperthyroidism give a clear history of the pre existent reaction picture This feature has more than academic significance After successful and complete surgical therapy the patient reverts to the state of autonomic imbalance whose manifestations must not be regarded as residual from the hyperthyroidism and in criticism of the surgical procedure

The Precipitating Factors—A variety of precipitating factors is encountered in the evolution of hyperthyroidism Most often there is a definitive history of a prolonged and insoluble emotional or psychic upset but occasionally the autonomic imbalance is activated by the more tangible factors of pregnancy acute infection an endocrinopathy or damage to the hypothalamus

The Phase of Hyperthyroidism—The phase of hyperthyroidism is initiated by widespread manifestations of psychic emotional and somatic disturbances The patient is usually tense anxious and unable to relax physically or mentally There is marked *emotional lability* Outbursts of anger and crying spells are easily provoked There is apt to be a continual *flight of ideas* and the powers of concentration are impaired producing a *mental chorea* *Insomnia* is constant distressing and quickly brings the patient to the point of complete exhaustion In attempts to sleep the individual twists and turns trying to find a comfortable position the mind races and the sensation of the pounding of the heart destroys any sense of surcease or security Mental aberrations phobias obsessions suicidal attempts and intense anxiety states are encountered especially at the onset of a thyrotoxic crisis In contrast to the agitated phases of hyperthyroidism an *apathetic* form is encountered especially in older pa

is an increased tendency to develop signs and symptoms of cardiac insufficiency

The circulatory status in hyperthyroidism resembles that of the normal person during exercise The changes are the usual physiological cardiovascular responses to the increased oxygen demands of the tissues *Cardiac output blood velocity and blood volume* are increased *Venous pressure* is normal unless there is backward failure An appreciable number of patients develop paroxysms of cardiac irregularity usually *auricular fibrillation* In a few of the older patients *cardiac invalidism* is the presenting syndrome and the classical symptoms of hyperthyroidism are conspicuously absent (*masked hyperthyroidism*) The importance of recognizing the significance of the basic metabolic disorder rests in the effects of subtotal thyroidectomy which may restore to normal the circulatory status

Tremor—Most patients exhibit a fine rapid tremor of the fingers which is apparent when the arms and hands are outstretched and the fingers are spread apart It becomes more obvious if a sheet of paper is laid upon the back of the outstretched hand It is also noted in the protruded tongue and may affect the lips and head In severe cases it may be universal and can be detected by palpating any voluntary muscle The origin of tremor is related to the generalized muscle weakness which is associated with creatinuria In addition to tremor twitching and choreiform movements may be encountered A few patients develop the *Parkinsonian syndrome* and there is an extraordinary increase in the incidence of a fibrositis of the shoulder producing the frozen shoulder See p 1505

Skin—The skin is warm and moist Hot flushes are common and are objective as well as subjective *Sweating* is profuse and generalized The palms are almost always red moist and clammy *Dermographism* is frequently seen and is related to the vascularity of the skin There is often some degree of *cutaneous pigmentation* which varies from a brown freckling of the extensor surfaces of the arms to a slight diffuse brown discoloration of the skin resembling that seen in Addison s disease The hair tends to become dry and lusterless and is apt to be prematurely gray

The Clinical Types of Hyperthyroidism —No two patients with hyperthyroidism present symptom complexes that are exactly similar Stated positively each patient with hyperthyroidism presents an individual symptom complex Plummer believed that the clinical types were caused by alteration in the thyroid molecule He differentiated between true hyperthyroidism resulting from an increased output of the normal thyroxin molecule and a dysthyroidism due to an increased output of an alterated thyroid molecule

Dysthyroidism (Plummer) —In dysthyroidism according to Plummer the patients were young exophthalmos was common the thyroid gland was diffusely enlarged the history of metabolic disturbance was of relatively short duration the response to iodine was favorable and the suggested surgical procedure was subtotal thyroidectomy

Hyperthyroidism or Toxic Adenomatosis (Plummer) —According to Plummer those with true hyperthyroidism or toxic adenomatosis were in the older group exophthalmos might be negligible or absent the history was of long duration the thyroid enlargement presented isolated nodules

thyroidectomy Occasionally it becomes extreme and is then termed malignant' When severe it becomes impossible to close the lids with resultant conjunctivitis drying of the sclera and corneal ulceration

The cause of exophthalmos in Graves' disease has never been satisfactorily explained It is certainly not thyrogenic in origin since it cannot be produced by the administration of thyroid It has been produced in guinea pigs by injections of anterior pituitary hormone and the ease of the production of exophthalmos in experimental animals is increased by thyroidectomy The best opinion regards exophthalmos as a manifestation of a hypothalamic disturbance although the mechanism of production still remains unknown

Goiter—Enlargement of the thyroid gland is often evident on inspection It is usually moderate in degree diffuse and symmetrical, but nodules may be felt due to the presence of cysts or adenomas Occasionally there is no evidence of enlargement in the anterior cervical region the entire gland being *substernal* and *intrathoracic* The consistency is somewhat rubbery A *systolic thrill* is palpable over each upper pole at the site of the superior thyroid artery and auscultation over this area reveals a *bruit*

The enlarged gland may cause pressure on surrounding structures The *trachea* may be narrowed and rotated with atrophy of the cartilaginous rings (*tracheomalacia*) Tracheal compression produces *dysphagia stridor hoarseness cough* and *dyspnea* In the presence of a substernal goiter there may be evidences of *superior vena caval obstruction*

Circulatory Phenomena—The *heart rate* is rapid ranging between 80 and 160 beats per minute At the time of a crisis the pulse rate may exceed 200 The degree of tachycardia roughly parallels the increase in basal metabolism The pulse is very labile mounting rapidly and excessively on slight exertion and excitement The excessive rate persists with little change during sleep in contrast to the tachycardia of psychoneurotics which is slowed In a few unusual cases despite an increase in the basal metabolic rate the pulse rate remains below 80 These patients with so called vagotonic Graves' disease probably had a normal resting pulse rate of 50 to 60 There is no true correlation between the degree of tachycardia and the presence or absence of palpitation

See *Differential Diagnosis of Tachycardia* (p 882)

Blood pressure readings reveal a constant increase in the pulse pressure due to a mild elevation of the systolic pressure but a striking decrease in the diastolic tension The latter is due to widespread dilatation of the peripheral arterioles in response to the increased oxygen requirements of the tissues A mild hypertension may subside with the relief of the hyperthyroidism More marked hypertension may be the presenting finding in masked hyperthyroidism'

See *Differential Diagnosis of Systolic Hypertension* (p 910)

The *heart* is usually normal in size but is manifestly overactive The sounds are loud and snapping The apical impulse is usually visible and diffuse and there may be a pseudostenotic thrill and murmur Diastolic and systolic murmurs are frequent particularly in the pulmonic area where the murmur may have a harsh quality of a friction rub In the presence of a complicating organic valvular or myocardial disease there

is an increased tendency to develop signs and symptoms of cardiac insufficiency

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presumably toxic adenomas, the symptoms were mild and commonly of cardiovascular origin, palpitation was frequent and was usually coincident with paroxysms of auricular fibrillation In some patients the whole picture was dominated by clinical evidences of cardiac failure and the other symptoms of hyperthyroidism were so mild as to escape notice (*masked thyrocardiacs*) The response to iodine was variable and might even be noxious The operative procedure was removal of the adenomatous nodule without necessarily reducing the surrounding nontumor tissue

The Unitarian Theory of Hyperthyroidism—The hypothesis on which *Plummer s differentiation* was based has never been proved It is our belief that the variations result from the altered response of the individual end organ to a fundamentally constant metabolic disorder In animals the response of the vascular system to a sympathomimetic drug produces an individual reaction picture that is as characteristic as the finger print In clinical autonomic imbalance the reaction picture is individual and identical and the individual reaction picture in clinical hyperthyroidism is the result not of differences in the deranged physiology but of the response of the individual tissue to a unitarian disorder The practical importance of the unitarian concept dwells in management If Plummer s hypotheses are accepted the primary and secondary cases of hyperthyroidism must be managed differently both medically and surgically If the unitarian concept is accepted the management of each patient is identical *Iodides are never contraindicated and are given with a reasonable prospect for a successful therapeutic result* The surgical procedure is never concerned solely with the removal of adenomatous nodules but is directed to the approach to subtotal removal of both tumor and nontumor tissue

Laboratory Findings—The laboratory findings of hyperthyroidism are no less distinct and widespread than the clinical manifestations

Basal Metabolic Rate—The basal metabolic level is increased the magnitude of the increase roughly paralleling the severity of the disease Readings of +30 to +60 per cent are common and the rate may exceed +100 per cent In establishing the true metabolic level the determinations are repeated on several successive occasions Aside from its diagnostic value the basal metabolism is of prognostic importance and is a valuable guide to the progress of therapy Only on rare occasions is the basal rate normal in patients with clinical hyperthyroidism Under such circumstances it must be assumed that the disease developed in an individual whose normal level was below average

See *Differential Diagnosis of Increased Basal Metabolic Rate* (p 720)

In apathetic types the basal rate may be high despite a calm exterior

Blood Chemistry—The *blood sugar* is usually normal but the *glucose tolerance* is impaired as indicated by a high prolonged glucose tolerance curve There is an appreciable incidence of complicating *diabetes mellitus* with some evidences of increased insulin resistance

The *blood cholesterol* tends to be low and is a better prognostic index than the basal metabolic rate since its level is calculated without the necessity of seeking the cooperation of the patient as in determinations of oxygen consumption

In the majority of patients the *blood iodine* concentration is increased

The average value is about twice the normal (6 to 12 gamma) with the principal increase in the organic iodine which probably represents thyro toxic iodine However the blood iodine may be normal or low in severe cases According to Cantarow the state of iodine metabolism is summar ized as (1) an increased mobilization of iodine from the thyroid gland (2) depletion of thyroid iodine (3) increased concentration of iodine in the blood (4) increased excretion of iodine in the urine feces and per spiration (5) negative iodine balance

The *blood calcium* and *phosphorus* levels are within normal limits but there is a negative calcium and phosphorus balance There is a specific diminution of *organically bound magnesium* in hyperthyroidism

The Urine—There is no obvious change in renal function although some patients have a mild polyuria and polydipsia The urinary excre tions of *iodine calcium* and *phosphorus* are increased There is spontane ous *creatinuria* which is undoubtedly related to the underlying disturb ance in muscle metabolism *Creatine tolerance* is constantly decreased After the oral administration of a standard test dose of 1 32 to 2 64 gm of creatine hydrate normal adults retain 75 per cent for twenty four hours whereas patients with hyperthyroidism excrete about 50 per cent in the urine

Liver function is often decreased and the liver itself is usually depleted of glycogen as manifested by hyperbilirubinemia decreased bromsulfalein excretion and impaired hippuric acid synthesis

Course—The spontaneous course of hyperthyroidism in the majority of patients is toward recovery but the *remissions* are interrupted by *ex acerbations* The spontaneous cycles of exacerbation and remission may be of greater or lesser severity They may be brief or protracted In a cer tain proportion of individuals vital organ damage either circulatory or hepatic terminates in chronic invalidism or death Occasionally the dreaded thyrotoxic crises are experienced with fatal termination

Complications—The complications of hyperthyroidism are many and varied Some are functional and others are somatic as in the liver and myocardium

The Thyrotoxic Crisis—The acute thyrotoxic crisis is attended by a mortality which varies from 50 to 90 per cent and is responsible for most of the fatalities in the disease The origin and explanation of these crises are even more obscure than those of the underlying disease

The crisis is characterized by a marked increase in all the pre existent symptoms of Graves disease The patient may be agitated to the point of mania or there may be coma and collapse Intractable vomiting and oliguria are common There is an alarming degree of hyperpyrexia and the temperature may rise to 107° F Extreme tachycardia cardiac irreg ularities and rise of blood pressure are invariably present

The crises are as unpredictable as they are violent They may occur early in the disease in individuals with mild unrecognized hyperthyroid ism as well as in those who are severely ill They may occur without an obvious provocative cause or they may follow an acute emotional upset an infection or a surgical procedure involving the thyroid gland or any other structure The incidence of postoperative crises has been greatly re duced by thorough pre and postoperative preparation

Mechanical Disturbances—Mechanical symptoms arise from the pressure of the enlarged thyroid upon the adjacent structures *Tracheal compression and vocal cord paralysis may be asymptomatic but occasionally* they cause aphonia dysphonia and dyspnea With large goiters of long duration *tracheomalacia* is a genuine surgical hazard since it leads to tracheal collapse after thyroidectomy

Malignancy—Malignant changes may occur in a goiter Statistics concerning the incidence of carcinomatous degeneration vary according to the criteria of malignancy employed *Many of the histologic phenomena* associated with malignancy may be observed in benign hyperplasia of the thyroid gland so that wary pathologists often refuse to commit themselves to a diagnosis on the basis of the microscopic evidence If epithelial changes without vessel invasion are accepted as evidences of malignancy then carcinoma of the thyroid is relatively frequent reasonably benign and amenable to surgical therapy and irradiation If the criteria of malignancy include the phenomena of invasion of vascular structures infiltration beyond the capsule and evidence of metastases thyroid malignancy is relatively rare highly malignant and therapy is all but futile The latter conclusion is in accord with our experiences Examples of malignant degeneration of hyperplastic and adenomatous thyroid glands have been of rare occurrence

Thyroid Apoplexy—Thyroid apoplexies may complicate hyperthyroidism The rupture of an artery is uncommonly seen in diffusely hyperplastic glands but occurs more often in old cystic goiters with markedly sclerosed vessels Thyroid apoplexy is one of the few painful thyroid afflictions It is readily diagnosed if suspected Therapy may be expectant since the thyroid capsule acts as a hemostatic

Heart Failure—Heart failure in hyperthyroidism is almost unknown before the age of twenty but increases in incidence after forty The older patients rarely have exophthalmos and the classical symptoms may be masked unless carefully sought in the elucidation of otherwise obscure cardiac invalidism and incapacitation At times failure results from the hyperthyroidism alone when the myocardium has been exhausted by the long duration of the disease More often the cardiac breakdown is precipitated by a paroxysm of auricular fibrillation prolonged hypertension or incidental arteriosclerotic rheumatic or syphilitic valvulitis *Often the* decompensation responds to the administration of iodine and permanent improvement follows thyroidectomy

Hepatic Cirrhosis—Jaundice and low grade liver damage leading to cirrhosis are late sequels of chronic hyperthyroidism The liver injury apparently is related to the depletion of the hepatic glycogen stores which increases susceptibility to toxic influences

Osteoporosis—The steady losses of calcium and phosphorus in the urine in prolonged hyperthyroidism produce a marked degree of generalized osteoporosis and pathological fractures occasionally occur

Paralysis Agitans—Long standing hyperthyroidism has been said to injure the basal ganglia and produce *paralysis agitans* More likely both afflictions are due to a hypothalamic lesion

Vitamin Deficiency—The hyperthyroid patient is constantly on the

verge of clinical vitamin deficiency Patients with hyperthyroidism not infrequently present evidences of vitamin A thiamine and riboflavin deficiency Many of the vague symptoms and signs of the disease may be related to this lack

Differential Diagnosis —Frank hyperthyroidism presents no difficulty in diagnosis Sympathomimetic manifestations and evidences of increased catabolism resulting in loss of weight and strength despite normal or increased alimentation suggest examination of the thyroid gland and estimation of the *basal metabolic rate* The *therapeutic test* of the response to iodine (p 1213) furnishes complete confirmation that clinical hyperthyroidism exists

Since determination of the basal rate requires the cooperation of the patient a strictly objective diagnostic test has been sought Goetsch attempted to utilize the *adrenalin response* for this purpose The presence of the adrenalin sensitivity in approximately 25 per cent of normal individuals and in a greater proportion of those with autonomic imbalance resulted in the abandonment of the Goetsch test More recently Shorr attempted to employ for diagnostic purposes the disturbance in *creatine metabolism* King and Soh al however question the specificity of the metabolic disturbance since it was demonstrable in normal individuals in patients with autonomic imbalance and might occasionally be absent in patients with frank hyperthyroidism The latter investigators concluded that clinical judgment surpasses in value any of these laboratory aids

Simple Goiter —It is comparatively simple to differentiate hyperthyroidism from simple thyroid enlargement whether diffuse or nodular hyperplastic colloidal or adenomatous Simple thyroid enlargement is unassociated with sympathomimetic activity or an elevation of the basal metabolic rate even when an anxiety state of goiterophobia is engrafted on the anatomical defect

Autonomic Imbalance —Patients with autonomic imbalance are all too frequently treated as sufferers from hyperthyroidism Clinical differentiation is based on the long standing history in simple autonomic imbalance the absence of clinical evidences of increased catabolism and the normal basal metabolic rate

Endemic Goiter and Autonomic Imbalance —Patients with autonomic imbalance who dwell in a goiter belt and present the combination of sympathomimetic symptoms and a lump in the neck with or without goiterophobia are almost certain to be told that they suffer from hyperthyroidism If the goiter is nodular the diagnosis of actual or impending toxic adenomatosis is suggested Determination of the basal metabolic rate is of inestimable value for it will be normal in the absence of clinical hyperthyroidism

Psychosis —Psychotic patients in manic phases may present a picture suggesting hyperthyroidism It is impossible to determine the basal metabolic rate under these circumstances It may require a prolonged period of study and a fine sense of clinical values to differentiate the two conditions The therapeutic response to iodine is an important differential consideration

Tuberculosis —Incipient pulmonary tuberculosis may simulate hyper

thyroidism to such a degree that chest roentgenograms are required for definitive diagnostication The presence of fever and a rapid sedimentation rate favor the tubercular process but both conditions may coexist

Masked or Occult Hyperthyroidism —Masked or occult hyperthyroidism occurs most commonly in older patients who are under medical observation for idiopathic hypertension or heart failure of unknown etiology They rarely present exophthalmos and the sympathomimetic manifestations may be mild and unrecognized To add to the diagnostic dilemma the thyroid enlargement may be negligible or the presence of the goiter may be missed if the swelling is retrosternal intrathoracic obscured by a beard or hidden beneath the muscles of the neck If the thyroid tumor is of long duration its importance may be discounted in the interpretation of the more recent symptomatology

This group of older patients presenting little exophthalmos and a long standing thyroid tumor correspond to Plummer s group of patients with secondary hyperthyroidism or toxic adenomatosis Despite the apparent surgical risk they tolerated well staged thyroidectomy often with spectacular clinical improvement

Treatment —The management of the patient with hyperthyroidism is a problem that has many facets Each patient presents a unique situation and management must be individualized

Autonomic Imbalance —The constitutional autonomic imbalance that underlies the clinical picture of hyperthyroidism is not amenable to specific therapy Preparations of belladonna ergot and quinine have been suggested and employed The use of *belladonna* and drugs of like action is pharmacologically incorrect since the paralyzant effect is upon the cholinergic (vagus) rather than the adrenergic system *Quinine* has no specific action on the involuntary nervous system and though widely used it serves no useful function *Ergot* and *ergotamine tartrate* are theoretically indicated but in practice these drugs have been disappointing We possess no modality that can successfully depress the tonicity of the adrenergic (sympathetic) nerves

Psychotherapy —The management of hyperthyroidism begins with the attempt to eliminate the factors that tend to precipitate exacerbation The most important of these is psychic trauma Commonly the psychic insult is characterological or situational It would be impracticable to summon a trained psychiatrist to aid in the solution of each clinical problem and in any event the internist or the general practitioner is usually aware of the difficulty A sympathetic understanding patience and a desire to suggest social and familial adjustments usually suffice to diminish the burden *The cooperation of the family fellow workers or employers is en*listed General hygiene is corrected so as to permit more rest The friction of everyday life is lessened by kindly and thoughtful advice When *the psychic trauma* is more deeply seated the help of a trained *psychiatrist* is advisable if not imperative but consultation is postponed until the metabolic abnormality has been corrected

Focal Infection —Focal infection as the excitant cause for exacerbations must be judiciously managed In the attempt to eradicate foci particularly in the sinuses or tonsils it is recalled that the thyrotoxic crises may be precipitated by operative interference anywhere in the body Con

sequently it is wise to postpone tonsillectomy for example until after thyroidectomy has been performed If it becomes necessary with the thyroid intact to eradicate a focus the same type of preoperative treatment as for thyroidectomy is employed

Institutionalization—The nonspecific management of the exacerbation requires institutionalization in order to procure mental and physical relaxation Except in the rarest of instances where the home is so luxuriously equipped that complete isolation is possible the patient with hyperthyroidism is referred for hospital care Patients and friends usually protest against hospitalization and suggest compromises such as rest at home or in the country but these alternatives invariably fail for some reasons

A *high calory high vitamin diet* is maintained in order to spare the tissues from the ravages of the excessive catabolism *Sedative therapy* by day and *hypnotics* at night assist in muting the nervous system

Professional nursing care at least during the day is almost mandatory An intelligent sympathetic and cheerful nurse should be chosen She should be taken into the confidence of the physician particularly concerning situational difficulties that have given rise to conflict between patient and relatives Often she tactfully manages the visitors who might otherwise be disturbing

The patient must not be permitted to chafe through idleness A daily schedule is established using hydrotherapy occupational therapy and visiting by appointment A haphazard conduct of the sick room defeats the purpose of the rest cure The radio for example is used for a limited time Under these circumstances it is quieting and sedative provided that amusing programs are chosen If turned on casually and left on indefinitely it becomes a nuisance

Specific Therapy—For the specific management of the exacerbation an infinite variety of therapeutic measures has been suggested Many of these have previously been discussed They include drugs such as *belladonna quinine* and the *ergots* glandular preparations such as *thymus extract adrenal cortical hormone androgen* and *estrogen* None of these possesses any specific therapeutic value Any improvement noted is probably manifestation of the spontaneous remissions characteristically seen in the disease

Antithyroid Drugs—A promising innovation in the conservative treatment of hyperthyroidism involves the use of *thio uracil* (deracil) The effectiveness of the preparation is due to inhibition of the manufacture of thyroid hormone When this action has proceeded to significant degree the pituitary may become more active with resultant hyperplasia of the thyroid and the paradoxical production of an increase in size of the goiter

Tablets of thio uracil (Deracil) are at present prepared in doses of 0 1 gm The initial daily dose may be 0 4 to 0 6 gm given in three divided doses Within a week of therapy the patient usually notices improvement but the most marked changes are not observed until the second third or fourth weeks When the basal metabolic rate has reached normal the daily dose of the drug is decreased to 0 2 or 0 3 gm After the expiration of two months if all is well it may be necessary to give no more than 0 1 or 0 2 gm in each twenty four hours The response to therapy is somewhat more rapid when iodide has previously been administered The remission may

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be maintained as long as the drug is continued On cessation of therapy a relapse occurs within a few weeks

Thio uracil may be used preparatory to thyroidectomy Under these circumstances the operation may be attended by slightly more bleeding and greater technical difficulty The preoperative thio-uracil response is abetted by conjoint iodide administration *The initial effect of the iodides* is noted in the period that transpires between the first administration of thio uracil and its most striking later effects on the basal metabolic rate Continuance of iodide therapy diminishes the extent of the goiterogenic action due to pituitary activity

Unfortunately, the administration of Deracil is not without danger Toxic reactions occur in 10 per cent of patients They consist of fever toxicoderms arthritis vomiting diarrhea enlargement of the salivary *glands edema of the legs lymphadenopathy, increase in the size of the* goiter leukopenia and agranulocytosis Blood dyscrasia offers a serious *barrier to the wider use of this otherwise effective preparation Blood* counts must be made at two or three day intervals whilst the preparation is being administered since progression of the leukopenia to the stage of agranulocytosis may result in a fatality The incidence of leukopenia may be reduced by oral doses of 200 mg of pyridoxin The treatment of agranulocytosis particularly with angina (p 1096), is most successfully conducted with penicillin and intravenous pyridoxin *(200 mg) A final hazard of* thio-uracil is its carcinogenic action not yet see in the human (p 572)

PROPYLTHIO URACIL (PROBACIL) —The search for less toxic substitutes for thio-uracil continues Promizole with similar anti thyroid activity seems more hazardous Thiobarbital in the smaller amounts of 50 mg is definitely less toxic but propylthio uracil in doses of 50 mg three times daily appears equally safe and more efficacious It may prove to be the preparation of choice though its administration must be safe-guarded with repeated *blood* counts *Iodides should* not be given with probacil

Roentgen Therapy—Roentgen therapy has been widely used for the control of exacerbations X ray treatments of the *thymic* and *anterior pituitary regions* are certainly of no specific value Irradiation of the *thyroid gland* has been employed by many workers notably Means and Holmes and is still widely utilized Hyperplasia of the thyroid gland is however in no way altered by irradiation Kessel and Hyman could find no appreciable difference in the course of patients treated by skillful neglect and *those who had been irradiated It is our opinion that the benefits that* follow roentgen therapy of the thyroid gland result from spontaneous remission or the psychotherapy that is so potent a nonspecific factor in all types of physical therapy

If roentgen therapy has any place in the management of hyperthyroidism its use should be reserved for *(1)* postoperative recurrences *(2)* juveniles *(3)* refusal of operation or *(4)* excessively bad risk subjects Employed when thyroidectomy is indicated irradiation therapy in our *opinion is* objectionable since the indicated operative procedure is delayed and made technically more difficult by the increased fibrosis and vascularity of the exposed tissue

The Use of Iodides—The rediscovery by Henry Plummer of the amazingly specific effect of iodine in the treatment of hyperthyroidism

constitutes one of the greatest of therapeutic achievements Iodine may be given by mouth inunction injection or inhalation The preparation may be organic or inorganic The dosage is conventionally 5 to 10 drops of Lugol s solution three times a day We are as ignorant of the correct dosage of iodine as we are of the mechanism by which the effect is obtained

INDICATIONS—It is our opinion that iodine should be given to every hyperthyroid patient whether of the so called primary or secondary types or whether the thyroid gland is diffusely enlarged or adenomatous since the specific effect of the drug is not dependent upon the histology of the thyroid gland We oppose the theory and practice of contraindication in so-called toxic adenomatosis

FAVORABLE RESPONSES AND THE THERAPEUTIC TEST—The response to iodine is used as a *therapeutic test* If patients are to be institutionalized the drug is withheld until hospital admission lest the improvement lead to the belief that ambulatory therapy is possible

The iodine reaction in hyperthyroidism consists of an extraordinary amelioration of symptoms The effect may be measured by diminution in tachycardia gain in weight and fall of the basal metabolic rate The relief of symptoms is initiated within twenty four hours to forty eight hours Normality can be approached in two to ten days

UNFAVORABLE RESPONSES (IODINE FASTNESS AND IODINE EXACERBATION)—The immediate and dramatic therapeutic result does not occur in all patients Occasionally the basal rate is unaltered and it actually may rise Many believe that these failures represent some altered reaction The terms *iodine fast* and *iodine exacerbation* have been employed to describe such instances It is our belief that the response to iodide in hyperthyroidism is always qualitatively the same The quantitative differences depend upon the phase of the disease that is present during therapy If the drug is administered at the onset of an exacerbation its effect will not be as obvious and dramatic as it would be if the patient were at the height of an exacerbation or at the beginning of a remission The iodine effect is determined by the specific action of the drug as modified by the violence of the exacerbation If the patient fails to improve with iodine therapy or the symptoms actually increase the drug is not stopped but increased dosage is employed while further search is made for the continued operation of provocative exciting factors particularly in the psychogenic sphere

DURATION OF FAVORABLE EFFECTS—The duration of iodine effect is variable and dependent upon the underlying character of the disturbance in the particular patient Many individuals with but slight evidences of hyperthyroidism are indefinitely maintained at normal by the continued use of the drug However those with moderate or severe hyperthyroidism whose spontaneous course is characterized by frequent and violent exacerbations may be held in a compensated state only long enough to permit them to be prepared for surgical procedure In these the drug is withheld until they are hospitalized lest the amelioration of symptoms encourage them to renege on the decision to submit to surgery Nor should the physician be influenced to a policy of conservatism by the favorable turn in events

Limitation of the use of iodine to preoperative preparation is in our

opinion erroneously conceived since many patients with mild disturbance are carried along indefinitely by the use of the drug The therapeutics of iodine in hyperthyroidism is a relatively simple problem that has been complicated by fanciful hypotheses having to do with iodine fastness 'iodine exacerbation and allegedly qualitative differences in response where adenomas are present

The mechanism by which the iodine effect is obtained is completely unknown A priori, one would expect iodides to be contraindicated and indeed from the writings of Trousseau to the notable contributions of David Marine this viewpoint was current in medical practice It remained for Marine to point the way for iodine therapy in hyperthyroidism and for Henry Plummer to popularize its use

While conservative therapy *including the use of iodine* almost invariably produces a remission exacerbations may be surely anticipated when the patient is returned to his normal environment and subjected to the stress and strain of existence

Radioactive Iodine—The use of radioactive iodine is still in an experimental phase It is impossible as yet, to state whether the property of radioactivity will accomplish more favorable responses in the alleviation of thyroidal difficulties than can be produced by the simpler preparations of the salt

Thyrotropic Factor—The experimental use of thyrotropic material is capable of producing a remission of the symptoms in hyperthyroidism Unfortunately prolonged administration of the hormone is capable of giving rise to antihormones creating a situation that is far too difficult for exploration by any but those thoroughly familiar with this complicated phase of clinical medicine

Surgery—Subtotal thyroidectomy offers the patient the quickest return to social and economic restitution and a minimal risk of later exacerbation It is our opinion that every patient with hyperthyroidism should be subjected to a thorough going subtotal thyroidectomy with the exception of the mild cases being controlled by iodine and thio uracil (Deracil)

THE TIME TO OPERATE—The time to operate is determined by the clinical course Postoperative difficulties are least if the procedure is done during a remission and greatest during an exacerbation or a period of increasing difficulty If preoperative therapy succeeds in an approximation to normal no great time is lost When circumstances permit we favor stealing the operation The time for operation is not disclosed to the patient o that the immediate panic and anxiety are allayed Oftentimes when very anxious and excitable patients become increasingly worse due to the suspense of anticipation the surgical procedure must be initiated earlier

ANESTHESIA—The patient is entitled to some form of *basal anesthetic* such as avertin by rectal instillation or an oral barbiturate such as Nembutal The use of an indifferent enema and colored lactose capsules for several days prevents the patient from realizing the significance of the administration of the basal anesthetic Avertin dosages may have to be high but the excess is syphoned off as soon as the patient goes off to sleep Our choice is the use of the oral hypnotic given in 3 or 4 times the usual dose The type of gas to be used can be determined by surgeon and anesthetist

THE TYPE OF PROCEDURE —The type of operative procedure must be settled between surgeon and practitioner before the patient enters the operating room There can be no question that nothing short of a subtotal thyroidectomy that leaves no more than one-tenth of the gland area should be the objective Arterial ligations hemithyroidectomy partial thyroidectomy and removal of adenomas constitute halfway measures which will be regretted sooner or later by all concerned The only debatable matter in our opinion is the problem of single or staged procedures

The staged operation has the lower morbidity and mortality It should be a matter of policy that if either surgeon or internist thinks the operation should be staged the more radical opinion should yield to the conservative opinion

The decision as to the staging of the procedure should not be made at the operating table More surgery than originally planned must not be done merely because things seem to be going well We favor the staged operation (*1*) For patients whose original basal metabolic rate is greater than +40 per cent (*2*) for those who have lost a great deal of weight and whose asthenia has been profound (*3*) for those whose basal metabolic rate cannot rapidly be brought to within twenty points of normal (*4*) for those who are highly agitated nervous and restless (*5*) for individuals whose skins are deeply pigmented (*6*) for older patients with definite evidences of vital organ damage in the liver or in the circulatory system (*7*) for those who have a persistent hypertension or who have had any type of mental disorientation and (*8*) for any patient who has ever had circulatory failure

The *first stage* of operation should rarely be less than a hemithyroidectomy If ligations are done the surgeon is faced with the alternative of more than two operations or a very formidable second stage procedure However if the patient takes the anesthetic badly or if paroxysmal cardiac irregularity of an alarming degree develops the operation must be stopped at whatever stage the difficulty may arise

POSTOPERATIVE CARE —Postoperative treatment should be initiated in the operative theater or at the latest immediately upon the patient s return to the bedroom An intravenous drip of 5 per cent glucose in saline is started whether or not indications exist After the first liter of fluid the solution is changed to 5 per cent glucose in distilled water since it is unwise to overload the patient with salt Iodine is to be given directly into the drip by rectum or if the patient is cooperative by mouth The dosage is difficult to estimate but it is common practice to use daily from 0.5 to 4 0 cc of Lugol s solution for the first few postoperative days The drip is maintained until the patient is wholly cooperative and well able to swallow fluids As soon as possible feedings and ante-operative medication are resumed

POSTOPERATIVE COMPLICATIONS —Many alarming complications may occur in the first few postoperative days The most serious of these is the *crisis* with or without paroxysmal cardiac irregularity and elevation of temperature The vast majority of postoperative crises are transitory and benign Expectant treatment with sedatives or narcotics and the continued intravenous administration of glucose saline and iodide (1 gm of sodium iodide in 20 cc) usually suffices to control the situation The

physician in his alarm must avoid the tendency to overmedicate The use of digitalis and stimulants such as caffeine camphor strychnine and coramine have possibilities only for harm It is well to remember that many patients with hyperthyroidism exhibit idiosyncrasy to morphine and are apt to vomit and become more agitated from the drug Sedation is better accomplished with the barbiturates or paraldehyde

When the temperature exceeds 104° F antipyretic measures are employed These include sponges packs and the use of the coal tars Oxygen therapy gives symptomatic relief and the cool temperature of a tent is most gratifying particularly if the weather is hot Kessel and Hyman in instances of ominous thyrotoxic crises used intravenous thyroxin in doses of 5 to 10 mg This has always been a measure of desperation based on the possibility that the removal of the thyroid tissue produced some type of insufficiency in the metabolic economy In a few instances we have had the clinical impression that a specific result was obtained This measure however is not to be employed *unless the situation is ominous* and the patient progressing unfavorably

The presence of a paroxysmal cardiac irregularity calls for the use of *quinidine sulfate* in 5 grain capsules every two three or four hours according to the patient s response *Digitalis* is contraindicated in every sense and may *add significantly to the burden*

Following operations on the thyroid *hemorrhage* is occasionally seen It usually comes from the superior inferior thyroid artery External bleeding is rare and the blood most commonly accumulates within the neck in a closed space beneath the pre thyroid muscles giving characteristic tracheal obstruction *Treatment consists of opening the wound and* evacuating the blood from beneath the pre thyroid muscles

Tracheitis is quite common after thyroid operation It is associated with a sense of irritation in the throat and the accumulation of mucous This tracheitis is treated by means of continuous steam inhalation

Injury to the recurrent laryngeal nerve occurs in about 0.5 to 2 0 per cent of cases of thyroidectomy *Unilateral nerve injury* is usually not followed by respiratory difficulty it may occur during operation or may not be noted until several hours later Any patient who develops hoarseness or difficulty with breathing should be subjected to laryngoscopy If bilateral paralysis is found the patient should be kept under very close observation and preparation is made for immediate tracheotomy if necessary

Postoperative tetany is due to removal of too much parathyroid tissue during the removal of the thyroid Symptoms of parathyroid deprivation usually first appear two or three days after operation The first symptoms are numbness tingling of the fingers and toes perhaps some stiffness of the face and hands Symptoms may rapidly progress to marked carpopedal spasm and rarely convulsions Diagnosis is confirmed by eliciting the Chvostek s or Trousseau s sign (p 724) and by the finding of a low blood calcium Response to intravenous injection of calcium gluconate 10 cc in a 20 per cent solution is dramatic In mild cases the symptoms are transient and the patient may be carried over the period of low parathyroid activity by adequate doses of calcium in the form of a gluconate by vein or the lactate by mouth for several days When symptoms are severe or

prolonged parathyroid hormone may have to be administered for long periods (p 1294)

CONVALESCENCE —Complications are encountered most frequently after subtotal thyroidectomy performed in one stage If the partial operation has been performed an interval must elapse before the completion of the subtotal thyroidectomy In convalescence after the complete operation or between the staged operations the patient is permitted to sit up and get out of bed as soon as the stitches have been removed and the temperature and pulse rates are normal A soft and then a full diet is advised immediately

We see no reason to wait more than ten days or two weeks between operative stages unless the condition of the patient makes it seem wise to temporize When patients are in fine condition an excessively long delay requires discharge from the hospital and readmission and the suspense and strain are not warranted The preparation for the second operation involves a return to the routine that preceded the first operation including the use of iodine

After the subtotal thyroidectomy has been completed the practitioner again resumes charge of his patient Iodine is continued in decreasing dosage for a long period of time in order to prevent hyperplasia of the thyroid remnant The daily dose may be reduced to 20 10 and then 5 drops of Lugol s solution and later the preparation need be given only five four and three days a week In the female the administration of iodine always is employed at the menstrual time

The patient must not attempt to resume a normal existence upon discharge from the hospital If possible there should be a period of convalescence preferably in the country The restfulne s and peace of mountain quiet for this purpose is superior to the more stimulating atmosphere of the seashore Upon return from convalescence the physician should discuss the patient s way of life in great detail Care must be taken that the physical and mental resources are not again strained Rest periods are interspersed in the course of the day or upon return from work The week end is used for convalescence and one day is well spent in bed The use of sedatives and hypnotics is continued and the basal metabolic rate is watched

When the subtotal thyroidectomy is adequate the majority of patients exhibit a low basal metabolic rate at the end of a few weeks or months If there are no associated conditions the patient need not be treated with thyroid extract If however the patient develops evidences of *cachexia strumipriva* thyroid extract is given in sufficient doses to approximate the basal rate to —10 per cent at which level the subjective symptoms should disappear Usually postoperative patients need more than the expected dose There is no advantage in using thyroxin intravenously or by mouth in preference to a good crude thyroid extract

Prognosis—The prognosis in hyperthyroidism today is universally bright Whereas twenty five years ago in the pre Lugol days the patient faced a surgical mortality approximating 15 to 20 per cent today a single operative death in a large series is a calamity that demands explanation This optimistic viewpoint must not be interpreted by general surgeons to indicate that the operative therapy of hyperthyroidism is lightly to be

approached The procedure though technically simple is too treacherous and dangerous to be attempted by the average surgeon who does an occasional operation A medical wag once stated the problem sagely when he said that 'no man should do a subtotal thyroidectomy until he has done a hundred' Furthermore the surgeon however competent should not attempt the management of these patients without the assistance and cooperation of an experienced practitioner If there is any problem in the field of medicine that requires teamwork and cooperation it is the management of the patient with hyperthyroidism

THE CLINICAL DISTURBANCES OF THE THYROID GLAND

In addition to the pathological physiological variations of hypothyroidism and hyperthyroidism the thyroid gland is subject to a variety of morphological variations which may or may not be associated with the systemic evidences of deranged glandular secretion The most important of these is endemic goiter an iodine deficiency Less frequently the gland is the site of congenital inflammatory neoplastic or vascular disturbances

CONGENITAL ANOMALIES

The thyroid gland is frequently anomalous A persistent *thyroglossal duct* may extend up to the foramen cecum at the posterior part of the tongue and require surgical removal for pressure symptoms or manifestations of growth that suggest malignant degeneration A nodule may remain at the base of the tongue or a portion of the duct may be pinched off in the neck and produce a *thyroglossal cyst* in the median line

Accessory thyroids are often found scattered throughout the neck Their anomalous situation and variations in arterial supply often cause technical difficulties during surgical procedures

SIMPLE OR ENDEMIC GOITER

The commonest disorder of the thyroid is a simple enlargement of the gland (goiter) that occurs in response to a lack of *iodine* Although it is unassociated with clinically demonstrable changes in function simple goiter may be a precursor of *cretinism myxedema hyperthyroidism* and *thyroid carcinoma*

Etiology—Simple goiter results from iodine deficiency Although it occurs sporadically throughout the world it is epidemic in certain regions where there is a low content of iodine in the soil and water These *goiter belts* include the Himalayan Mountain region of South Central Asia the Alps Pyrenees and Carpathian Mountain regions of Europe the Andean Plateau and Southeastern Brazil in South America the Saint Lawrence and Great Lakes basin extending through Minnesota the Dakotas and adjacent Canadian provinces and the Pacific Northwest including Oregon Washington and British Columbia In this country the disease is rare along the Atlantic Coast and Gulf of Mexico

A number of physiological influences are capable of inducing a *relative iodine deficiency* and are largely responsible for sporadic instances which occur when there is adequate dietary iodine The needs of the body for iodine are increased by *puberty pregnancy* the *menopause infections* and *exposure to cold* and *high altitudes* The absorption and utilization of an adequate dietary intake of iodine are impaired by vitamin A deficiency a diet rich in *vegetables of* the cabbage and cauliflower variety (containing appreciable cyanide) and a high calcium content of drinking water

Pathology—The pathology of the goiter is dependent upon the *iodine storage* in the colloid With minimal amounts there is pronounced *hyperplasia* The cells are hi lumnar

the lumen is obliterated by the invaginations of the lining epithelium vascularity is increased and colloid secretion is absent When iodine storage is resumed the gland involutes to a *colloid or resting stage* with flat cuboidal cells a wide lumen and a rich supply of colloid in the lumen

The stage of *colloid goiter* represents physiologic compensation as a result of (1) increased iodine intake (2) increased secretory epithelium or (3) decreased demands upon the organism The completely involuted thyroid (colloid goiter) is the closest condition to normal physiologically chemically and anatomically that a thyroid that has once been actively hyperplastic can again resume (Marine) Resumption of iodine deficiency produces a *colloid-hyperplasia* and this interplay may go on indefinitely Sooner or later small islands of tissue become separated and form *cysts* or *adenomas* These alternate likewise between hyperplasia and colloid involution forms but lag behind the nontumor tissue in their metamorphoses since they are functionally less active

This dynamic concept of the morphology of the thyroid emphasizes the misleading nature of separate clinical concepts of colloid goiter cystic goiter adenomatous goiter nodular goiter and so forth

Clinical Manifestations —Endemic goiter occurs in all races and in all climates It develops more frequently before sexual maturity and is most common during gestation puberty pregnancy lactation and at the menopause It is more common in females after puberty but in endemic regions there is no appreciable sex difference

At the onset the enlarged gland is soft and symmetrical Variations in size are not infrequent especially with iodine therapy (*iodine thyroiditis*) during pregnancy and at menstruation Some patients show signs of mild hypothyroidism indicating a degree of *exhaustion atrophy* Goiters of long standing tend to become *cystic* and *adenomatous* In the latter *pressure symptoms* are commonly met with as manifested by dysphagia cough hoarseness and aphonia More often the patient develops a goiterophobia The visible lump in the neck awes the victim whose fears are intensified by threats of suffocation and the bruited dangers of developing toxicity and malignant degeneration Surgeons in their furor operandi often fan these fears to the point that thyroidectomy is demanded

Endemic Goiter Hyperthyroidism and Malignancy —It is our opinion and experience that the patient with endemic goiter has no more or less chance of developing hyperthyroidism than the non goitrous The symptoms of excessive thyroid function are no commoner in goiter belts than at the sea coast We are in disagreement too as to the incidence of malignant degeneration of the goiter It is nowhere near the quoted figures of 2 to 3 per cent In twenty five years of practice we have seen but one in our office Nor do we agree that the nodular appearance or feel of the gland carries the threat of toxic adenomatosis

Endemic Goiter and Cretinism —In endemic areas several generations of simple goiter lead to cretinism Goiter is the first stage on the road to cretinism (Morel) Occasional cases of myxedema arise from the exhaustion atrophy of a simple goiter Thyroid apoplexy is rare and violently painful

Treatment —The *prophylaxis* of endemic and sporadic goiter is accomplished by the administration of *iodine* in any form and by any means The required dose varies in different districts with different age groups with diet and climate The addition of 10 mg of potassium iodide per kilogram of table salt (1 100 000) is suggested or 3 to 10 drops of Lugol s solution may be given a few days a week or a few weeks each year Rou

tine goiter prophylaxis results in a decreased incidence of cretinism a decrease in necessary thyroid surgery and a decline in the occurrence of benign tumors of the thyroid

Simple goiter is cured if iodine is administered in the early hyper plastic stage Sodium or potassium iodide is given in doses of 10 to 15 mg once daily during alternate months for a year A maximum regression of the goiter occurs in about a year if therapy is continuous In long standing hyperplasias with colloidal cystic and adenomatous changes iodine ther apy cannot be expected to reduce the size of the gland but prevents in crease in size due to resumption of hyperplasia

Iodine Basedow —The concept of Iodine Basedow s disease implies the activation of the simple goiter to a stage of hyperthyroidism as the result of iodine administration We do not deny that an occasional patient with endemic goiter may develop hyperthyroidism while exposed to iodine but we do not believe a causal relationship exists We entertain no fear in our administration of iodine in the prophylaxis and control of goiter and have yet to regret that policy

Surgery —The surgery of simple goiter is limited to cosmetic proce dures and those aimed at relief of pressure symptoms We do not regard as indications the prophylaxis of hyperthyroidism toxic adenomatosis or malignancy

HYPERTROPHY AND HYPERPLASIA

The histological picture of hypertrophy and hyperplasia of the thy roid gland has no specific connotation The statement that this appearance characterizes *hyperthyroidism* is no longer tenable since it is observed in *endemic goiter* (p 1218) and *cretinism* (p 1191)

Hypertrophy and hyperplasia of the thyroid gland imply nothing more than deficient storage of iodine in the thyroid colloid This may be due to dietetic errors as in endemic goiter or depletion of the hormone as in states of hyperthyroidism and in myxedema *Treatment* with iodine pro duces reversion to colloid and may prevent the formation of adenomas and malignancy

THE COLLOID GOITER

The colloid goiter is one in which there has been a previous hyper plasia and hypertrophy due to iodine deficiency and a compensation with adequate storage The colloid appearance may be found in normal sub jects in endemic goiter or in patients with hyperthyroidism who have received large doses of iodides The colloid change may occur in the non tumor tissue of the gland or in the adenoma The latter being functionally less active takes up iodide with less avidity than the nontumor tissue so that there is the occasional appearance of colloid non umor tissue with a hyperplastic adenoma

The colloid gland representing an approximation to normal requires no therapy other than the prevention by iodine of recurrent hyperplasia

ATROPHY

Atrophy of the thyroid gland is most often an *exhaustion effect* and follows prolonged hypertrophy and hyperplasia (p 1220) With symptoms of hypothyroidism the administration of *thyroid extract* is indicated

CACHEXIA STRUMIPRIVA

Accidental cachexia strumipriva is the term used to describe myxedema occurring in patients who have had a thyroidectomy for a simple nontoxic goiter or hyperthyroidism In either instance substitution therapy with a potent thyroid extract is required *Therapeutic* cachexia strumipriva is de liberately induced for the relief of cardiac invalidism and persistent angina (p 890)

ADENOMA OF THE THYROID GLAND

The thyroid gland like other glandular structures often reveals mul tiple areas of benign adenoma Glands that have been the site of a long standing hypertrophy and hyperplasia are more prone to show these adenomatous areas Those who follow the teachings of Henry Plummer regard adenomas as potentially toxic

TOXIC ADENOMATOSIS (TOXIC NODULAR GOITER)

Toxic adenomatosis of the thyroid gland as described by Plummer consists of a syndrome that is more often encountered in elderly patients Usually there is a long standing history of a simple goiter with a slow on set of toxicity In these patients there is rarely exophthalmos but cardio vascular difficulties are frequent Dr Plummer believed that iodide was contraindicated in this group since it was likely to cause an exacerbation of symptoms It was his viewpoint that removal of adenoma sufficed to relieve the syndrome without greatly sacrificing the nontumor tissue

The divergent opinion however with which we ourselves agree credits the differences in the syndrome not to an altered molecule but to the dif ferent response of the older patient Exophthalmos is not usually encoun tered in those who develop the disease after the age of thirty five It is natural to expect that the older group will develop more cardiovascular difficulties The responses to iodine in our experience are similar to those seen in the younger group Believing that a satisfactory result cannot be obtained by removal of the adenoma alone we favor the use of preopera tive iodinization in these cases and the performance of subtotal thyroid ectomy

CARCINOMA OF THE THYROID GLAND

The problem of cancer of the thyroid is almost as controversial as that of the adenoma The difficulties rest in the histological picture In many cases in which there is intense hyperplasia the histological appearance suggests malignancy but the clinical course belies the ominous sentence of the microscopist Clinicians relying on the pathological report issue rec ords of the great frequency of the malignancy and remarkably successful results of therapy

It was this histological difficulty that led to considerable confusion in experimental work The thyroid cancer of brook trout which was sub jected to exhaustive studies was found to be a marked hyperplasia which responded to the administration of iodine The result of these observa tions led many pathologists to be unwilling to render an opinion as to malignancy from the appearance of the microscopic slide alone

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With true malignancy of the thyroid, a complete *surgical dissection* is followed by intensive *roentgen therapy* In our experience the outlook is exceedingly poor since it is all but impossible to remove or destroy the cancerous tissue

CYSTS AND CYSTADENOMAS OF THE THYROID GLAND

Cysts of the thyroid gland occur sooner or later in most hyperplastic hypertrophic glands whether in the nontumor tissue of the gland or in an adenoma Under the latter circumstance the condition is described as a *cystadenoma* Provided that there are neither toxic nor mechanical symptoms cysts and cystadenomas do not require surgical excision unless for cosmetic reasons

INFLAMMATIONS

Inflammatory disturbances of the thyroid gland are of rare occurrence When they are encountered in the normal gland the condition of *thyroiditis* or *perithyroiditis* results Inflammation of a goitrous gland produces a *strumitis* In all likelihood the inflammatory thyroid lesions are vascular in origin and in the nature of a *perithyroiditis*

Thyroiditis.—Thyroiditis is an unusual condition but it may result from invasion of the gland by a pyogenic microorganism The symptoms consist of local pain tenderness thyroid swelling and obstruction to the trachea Ordinarily the process subsides spontaneously as the result of local application of cold With obstructive symptoms operation is necessary for purposes of decompression Antithyroid drugs merit trial (p 1211)

Strumitis —Inflammation of the goitrous gland produces a peculiar and unusual type of ligneous reaction which bears the name of Riedel who first described it *Riedel s disease* is probably identical with *struma lymphomatosa* or *Hashimoto s disease* These conditions are rare and when observed occur in women beyond middle age The gland is smooth uniform and firm and there is a gradual onset of the symptoms of myxedema Microscopic examination is required to ascertain the nature of the process Antithyroid drugs merit trial (p 1211)

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The intense vascularity of the hyperplastic and hypertrophic thyroid gland has been previously described In goiters of long standing *thyroid apoplexy* is encountered due to the rupture of a brittle vessel as the result of exertion and increase in systemic vascular tension The bleeding is usually arrested by the pressure within the thyroid capsule and it may cause tracheal compression

Conservative treatment using local cold packs usually is sufficient unless the respiratory symptoms call for surgical decompression This is distinctly a procedure for the operating room since hemostasis may present a considerable problem after the gland capsule has been incised

THE PARATHYROIDS

The parathyroid glands consist of four oval structures about 6 mm in length usually situated on the dorsal surfaces of the thyroid lobes More often than not the anatomical structure is atypical and aberrant parathyroids may be situated as far down as the apex of the lung and as far back as the esophagus The glandular tissue consists of solid masses of large round cells separated by capillary sinuses The clear *chief cells* which have large nuclei and poorly stained cytoplasm produce *parathyroid hormone* The larger *oxyphile cells* contain eosinophilic granules and do not occur in the human glands until the age of ten The blood supply of the glands is derived from the inferior thyroid arteries and functional activity is controlled by the *anterior pituitary hormone*

Physiological Considerations.—The chief function of the parathyroid glands is to provide a normal concentration of calcium and phosphorus in the body fluids The mechanism by which this is accomplished is not completely understood but it involves the maintenance of an equilibrium between the excretion of these electrolytes their absorption from the intestinal tract and their deposition and liberation from bone

Removal of the parathyroid glands results in a decreased elimination of phosphorus in the urine retention of phosphorus an increase in the inorganic phosphorus of the serum and a decrease in its calcium content The alteration in the electrolyte composition of extracellular fluid leads to the production of the symptom complex of *tetany* (p 723)

The presence of an excess of parathyroid hormone in the body (as a result of a parathyroid tumor or from an excessive injection of a potent parathyroid extract) produces a decrease in the serum inorganic phosphorus concentration an increased renal excretion of calcium and phosphorus an appreciable diuresis a rise in the serum calcium concentration chiefly due to an increase in the ionized fraction and decalcification of the bones

In the presence of increased parathyroid function calcium administered by mouth tends to remain in the blood stream and produces significant *hypercalcemia* until excreted in the urine

Physiological increases in parathyroid activity accompanied by evidences of parathyroid hyperplasia are encountered in response to calcium deficiency or hyperphosphatemia in order to maintain a normal level of calcium and phosphorus in the serum Such physiological hyperparathyroidism may be seen during pregnancy where the maternal skeleton may be demineralized to meet fetal demands in rickets in chronic renal disease and in destructive lesions of bone

The manner in which the parathyroid hormone acts is poorly understood There is some evidence that the hormone acts directly on the kidney since diuresis and an increased elimination of phosphorus are among the first effects to be noted Apparently the parathyroid hormone can affect the activity of the bone cells Large doses stimulate the osteoclasts and produce resorption of bone and fibrosis a condition known as *osteitis fibrosa cystica* (p 1225) Small doses induce an osteoblastic effect leading to the formation of hard sclerotic bone (osteosclerosis)

Pharmacology.—Parathyroid hormone is prepared from beef parathyroids by acid extraction and iso electric precipitation The resultant extract

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damaged either from the electrolyte disturbance or a direct nephrotoxic effect of the hormone A rise in the blood phosphorus and nonprotein nitrogen heralds the onset of renal insufficiency Death from acute renal insufficiency has been known to occur quickly after parathyroid over dosage Where overdosage is protracted abnormal deposits of calcium oc cur in the soft ti sues nephrolithiasis develops and osteitis fibrosa cystica occurs

HYPERPARATHYROIDISM

Hyperparathyroidism is characterized by an increased renal excretion of calcium and phosphorus hypercalcemia hypophosphatemia skeletal decalcification and the deposition of calcium in the soft tissues and the urinary passages Its presence is suggested particularly by the association of urolithiasis and chronic bone disease or multiple fractures

Etiology —Hyperparathyroidism occurs in primary and secondary forms *Primary hyperparathyroidism* usually is due to an *adenoma* of one of the glands and less commonly to idiopathic hyperplasia of the parathyroid apparatus The *secondary* variety is the result of a compensatory hyper plasia which occurs in association with a variety of disturbances such as rickets osteomalacia multiple myeloma skeletal carcinomatosis Cushing s syndrome and chronic renal insufficiency

Pathology —The essential pathology of hyperparathyroidism is revealed in the glandular skeletal and renal tissues

The Parathyroids —In hyperparathyroidism the parathyroid l sion is an adenoma of on or more glands or a generalized hyperplasia The *adenomas* vary greatly in size but are usually no la ger than a small bean although large tumors the size of a small orange have been encountered The tissue appears brownish red and usually consists almost entirely of ch ef cells although some tumors contain large numbers of oxyphile and transitional cells Failures to find the parathyroid adenoma at operation or at autopsy are frequent and are due to variability in the numbers and positions of the gland Adenomatous parathyroids have been found in the anterior and posterior mediastinum at the base of the tongue in the retro-esophageal region an l within the thyroid gland

Primary parathyroid hyperplasia is usually unequal one or more glands being larger than the others In id opathic hyperplas a the dominant cell is the *ch ef* cell and the glands retain the r *reddish brown* color In the *secondary type* as seen in patients with chronic renal d sease the hyperplastic glands appear *yellow* and are compos d of water clear cells When a parathyroid adenoma is complicated by chronic renal insufficiency the glands may show a combination of chief ell adenoma and water clear hyperplasia

Osteitis Fibrosa Cyst ca —In early hyperparathyroid sm the skeletal changes consist of a general zed osteoporosis with replacement of the resorbed bone by fibrous tissue containing a mod rate amount of primitive poorly calcified new bone Microscopically the process is reflected by increase l numbers of osteoclasts and the p esence of many deep lacunae The *n rmally bony architecture becomes extensively changed unt l there is little evidence of the* original osseous structure Large fibrous s ars which replace the original spongiosa and cor tex give rise to larg cystic areas easily seen on radiographs Some degree of cortical thick en ng occurs on the medullary s de as seen best in the calvarium

The skel tal changes are attended by a softening of the bone and the occurrence of *multiple fractu es Deform ties* are produced by faulty position and excessive callus forma t on The vert bral column the long bones and the pelvis which are subjected to the great est funct onal stress and stra n are usually the most extens vely involved Severe atrophic changes occ ır in the terminal phalanges and lead to the formation of *clubbed fingers* As a result of involvement of the jaws the teeth loosen and fall out The *permanent teeth do* not share in the gen ral decal fcation but the develop ng teeth show defective dentine for mat on The cortice of the jaw bones are frequently expanded by cysts wl ich give rise to the ep lis a tumorl ke ma s

Re al and Other Lesions —In primary hyperparathyroidism calcium depos ts are found

is crude, protein in composition and readily inactivated by acid or alkaline hydrolysis and proteolysis Hydrolysis with weak acid produces an increase in free amino groups and a decrease in activity

Preparation and Assay—*Solution of parathyroid* is official in the United States Pharmacopeia XII Its *activity is determined by bioassay* on normal male dogs weighing 8 to 16 kg One hundred units represents the amount of hormone activity necessary to raise the serum calcium level one mg per cent within 16 to 18 hours after subcutaneous injection

Preparations are adjusted to contain 100 units per cubic centimeter

Mode of Administration—Parathyroid extract must be given parenterally since its activity is destroyed by proteolytic enzymes in the digestive tract *It is usually administered subcutaneously In an emergency it may* be given intravenously The specific effect is not manifest for three to six hours and may not become maximal until eighteen hours The duration of the effect may approach thirty six hours The simultaneous use of acidifying salts such as an acid ash diet calcium salts and vitamin D enhances the potency and toxicity of the extract

There is a great variability in the intensity of the individual response to the hormone Amounts that will markedly elevate the blood calcium in one individual may have little effect in another Repeated small doses are more effective than a single large injection After several months of use an *immunity to parathyroid extract is established* and enormous doses may produce practically no effect This is probably an antibody reaction due to the protein present in the extract

When using parathyroid extract dosage should be controlled by frequent blood calcium determinations and the careful evaluation of renal function

Therapeutics—Parathyroid extract has a very limited scope in clinical *practice The effects of the hormone in the production of hypercalcemia* and hypophosphatemia may be obtained with great consistency and safety by using calcium salts or *dihydrotachysterol (A T 10)*

The dangers and drawbacks inherent in parathyroid therapy include the uncertainty of its effects the immunity that develops to continued administration the possibility of causing damage to renal function and the necessity for repeated administrations of the hormone at intervals that can only be defined with accuracy by knowledge of the blood calcium level

In an acute tetany such as occurs following thyroidectomy or the removal of a parathyroid adenoma it is wiser to rely on intravenous injections of the calcium salts oral doses of calcium and vitamin D and limitation of the intake of phosphorus At the same time dihydrotachysterol may be administered orally with considerable safety In chronic hypoparathyroidism similar measures are of equal efficacy with lesser risk

The nonspecific use of parathyroid extract has been suggested in the treatment of edema lead poisoning radiation sickness allergy and thrombocytopenic purpura The results have not been impressive though an occasional success has been reported

Toxicology—When given in excess parathyroid hormone produces a characteristic group of toxic phenomena There is a marked increase in the blood calcium level which may reach 18 to 20 mg per cent The kidney is

Malpositions of the broken bones which heal rapidly lead to *irregular deformities* Localized defects are caused by the formation of *cysts* and *bone tumors* The skull may become enlarged and takes on the appearance of an *osteitis deformans* (p 2879)

Urinary Symptoms—The increased urinary excretion of calcium and phosphorus is attended by a *polyuria* due to the osmotic effect of the dissolved electrolytes and a direct diuretic effect of the hormone on the renal parenchyma The renal loss of fluid is augmented by progressive but mild renal insufficiency and as a result *polydipsia* and *nocturia* are additional complaints

Renal calculi are almost always present It has been estimated that 5 per cent of all patients with urolithiasis are afflicted with hyperpara-



Fig 252—X ray of the femur showing the rarefaction and expansion of the [illegible] trabeculation characteristic of osteitis fibrosa cystica

thyroidism The calculi are usually bilateral and often form staghorn casts of the renal pelvis They are composed of calcium phosphate and are radiopaque Some patients with renal calculi have little other objective evidence of hyperparathyroidism although surgical exploration results in the demonstration of a small adenoma

Dysuria frequency urgency hematuria and repeated attacks of *renal colic* are common results of the calculus formation which predisposes to urinary tract infection and renal insufficiency

The Clinical Manifestations of Secondary Hyperparathyroidism.—From a clinical standpoint secondary hyperparathyroidism is important only in patients with chronic renal disease In *multiple myeloma* (p 1126) *rickets* (p 2850) *osteomalacia* (p 2853) and *metastatic skeletal carcinomatous*

in the kidneys *Nephrocalcinosis* is mainly peritubular and tends to obstruct the lumen until *renal calculi* are formed to shape complete casts of the renal pelvis *Pyelonephritis ureteritis* and *cystitis* are frequent complications of the urolithiasis and the continued effects of these several factors eventually lead to chronic renal insufficiency

Metastatic calcium deposits also occur in the myocardium endocardium the muscularis and intima of the arteries about the large joints and in the subcutaneous tissues

Pathogenesis—The mechanisms by which excessive parathyroid hormone is secreted vary in the primary and secondary types of hyperparathyroidism

Primary Hyperparathyroidism—The essential defect in primary hyperparathyroidism is the excess of parathyroid hormone in the body fluids In the presence of intact renal function the hormone increases the urinary excretion of calcium and phosphorus probably as a result of a direct action on the renal cells The negative mineral balance is attended by augmented activity of the *osteoclasts* which cause progressive resorption of bone replacement fibrosis and cyst formation (*osteitis fibrosa cystica*) The dissolution of bone is reflected by the increase in serum calcium and phosphatase The saturation of the blood and urine with calcium and phosphorus favors the formation of calcium deposists in the soft tissues and urinary passages The classical features of hyperparathyroidism have been reproduced in experimental animals by prolonged and repeated administrations of parathyroid hormone

Secondary Hyperparathyroidism (Renal Rickets)—In secondary hyperparathyroidism as seen in patients with chronic renal insufficiency the retention of inorganic phosphorus incidental to impaired renal function stimulates the parathyroids to increased activity The osseous changes are particularly in evidence as indicated by the use of the term *renal rickets* but there is a lesser tendency to urolithiasis since the impaired kidneys hold back the calcium excess

Clinical Manifestation of Primary Hyperparathyroidism—The onset of primary hyperparathyroidism is usually insidious and many years of vague ill health precede the recognition of the underlying disease The diagnostic possibility often is first suggested by the occurrence of one or more *pathological fractures* attacks of *renal colic* or the appearance of an *epulis* Less commonly the onset is abrupt and the course fulminating with severe constitutional symptoms resembling the effects of an overdose of a potent parathyroid extract (acute hyperparathyroidism) The symptoms and signs in either event are largely the result of hypercalcemia skeletal decalcification and the increased urinary excretions of calcium and phosphorus

Hypercalcemia—The serum calcium is usually elevated and may rise to 16 to 18 mg per cent Hypercalcemia of this degree regardless of the actual cause produces *generalized weakness adynamia anorexia nausea vomiting abdominal pain* and *cardiac irregularities* Extreme hypercalcemia (18 to 20 mg per cent) may produce intractable nausea vomiting and diarrhea culminating in severe shock The latter symptoms are prominent in *acute parathyroid poisoning*

See *Differential Diagnosis of Hypercalcemia* (p 723)

Osteitis Fibrosa Cystica—The generalized osteoporosis is commonly attended by aching *pain* in the back and extremities The pain is of a deep boring type and may become sufficiently severe to impede movement Collapsed vertebrae compressing the spinal nerve roots give rise to excruciating lightning pains although it is not unusual for hyperparathyroid patients to be free from bone pain in spite of extensive skeletal lesions

Gross alterations in skeletal form occur as a result of softening cyst formation and bone replacement The progressive collapse of vertebrae produces a marked *kyphosis* (p 3062) and a resultant decrease in height *Fractures* are frequent and occur in response to minor stresses and strains

Blood —The principal blood chemical changes are *hypercalcemia hypophosphatemia* and *increased serum phosphatase* activity *Serum calcium* values are usually between 12 and 14 mg per cent but may rise to 20 mg per cent The *inorganic phosphorus level* is moderately depressed to 1.5 or 2.5 mg per cent while *serum phosphatase* activity is increased four or five fold to 15 to 30 Bodansky units or 40 to 60 King Armstrong units

See *Differential Diagnosis of Hypercalcemia* (p 723)

The elevated serum calcium is due to an *increase in the ionized fraction* In the interpretation of calcium values it is important to check the total protein concentration since patients with hypoproteinemia reveal normal figures for total calcium despite a significant increase in the ionized fraction A second factor of great importance in the interpretation of serum calcium levels is the value for inorganic phosphorus In patients with inadequate renal function hyperphosphatemia depresses or prevents hypercalcemia A normal calcium value (10 to 11 mg per cent) in the presence of an increase in inorganic phosphorus (5 to 8 mg per cent) is highly suggestive of hyperparathyroidism The reciprocal relation between calcium and phosphorus levels is often indicated by the prompt reappearance of hypercalcemia when therapy directed at the renal insufficiency lowers the inorganic phosphorus value

See *Differential Diagnosis of Hypophosphatemia* (p 728)

The blood *levels show wide fluctuations which tend to parallel the* activity of the disease but there is no correlation between the blood figures and the extent of the skeletal lesions There is some evidence that *the level of serum phosphatase activity is an index of the intensity of the* disease although in long standing disturbances the composition of the serum may not be greatly altered

See *Differential Diagnosis of Increased Phosphatase Activity* (p 728)

Urine —The urine is dilute pale of large volume and contains excessive quantities of calcium and phosphorus A gross demonstration of the excess of urinary lime is provided by mixing equal quantities of urine and a buffered ammonium oxalate solution (*Sulkowitch s reagent*) which consists of 2 5 gm of oxalic acid 2.5 gm of ammonium oxalate 5 cc of glacial acetic acid and distilled water to make 150 cc A heavy white precipitate of calcium oxalate testifies to the nephrocalcinosis

Actual determination of *urinary calcium excretion* is of great diagnostic value The patient is placed on the Bauer Aub low calcium diet which provides 100 mg of calcium daily This is continued for two three day periods and the total twenty four excretion of calcium is determined each day In normal patients on this diet the urine contains 60 to 80 mg of calcium per day but in hyperparathyroidism the daily excretion of calcium may reach 500 to 1000 mg Calcium balance studies are valueless in the presence of renal insufficiency and may be misleading in patients with calcium phosphate renal calculi

Microscopic examination of the urine frequently discloses white blood cells red blood cells and casts Many specimens show *calcium phosphate* casts which readily dissolve in 2 per cent acetic acid These are seen more commonly in hyperparathyroidism than in any other condition

Stool —The stool calcium is normal in hyperparathyroidism as long as renal function remains adequate In the presence of renal insufficiency

(p 572), the disturbance is essentially of academic interest and there are no clearly defined clinical features specifically related to the hyperfunctional state

Renal Rickets Renal Dwarfism—The hyperparathyroidism of renal disease is seen in children and adults who suffer from protracted slowly progressive *renal insufficiency* (p 2275) In children, the causative kidney lesion may be in the nature of a congenital anomaly (p 2296) or a long standing chronic nephritis The resultant syndrome has been designated as *renal rickets renal osteodystrophy renal dwarfism* or *renal hyperparathyroidism* It is commonly seen during the second decade and progresses slowly to a fatal renal failure The osseous changes are similar to those of rickets but cannot be differentiated histologically from those of primary hyperparathyroidism Thickening of the epiphyseal cartilages swelling of the ankles and wrists and deformities of the spine and extremities are



Fig 253—Renal calculus in pelvis forming a complete mould of all the calyces (staghorn cast) and extending into the ureter

encountered There is marked stunting of growth and all other phases of development producing the state of *renal dwarfism* The urinary symptoms of nephrocalcinosis are minimal due to the inability of the damaged kidney to excrete the excess of calcium

Renal hyperparathyroidism in adults is usually a terminal phase of renal insufficiency The underlying renal lesion is commonly a *chronic nephritis bilateral congenital polycystic disease* or *renal lithiasis* with *chronic hydronephrosis* and *pyelonephritis* Often there is only a slight generalized osteoporosis but extensive osseous changes which are indistinguishable from osteitis fibrosa cystica have been observed

Laboratory Data—Evidence of hyperparathyroidism is afforded by examinations of blood urine and stool and by radiographs of the bones and kidney regions

porosis without cyst formation Blood chemical figures are normal in contrast to the distinctive pattern in hyperparathyroidism (p 1225)

Treatment

The treatment of *primary hyperparathyroidism* consists of surgical removal of the offending tissue The extirpation of the glands in *secondary types* is contraindicated in view of the compensatory nature of the hyperplasia Diets rich in calcium phosphorus and vitamin D do not retard the progressive decalcification of the active disease Indeed this type of regimen is nephrotoxic and increases the severity of the renal lesion Large amounts of calcium may produce a sharp increase in the degree of hypercalcemia with its attendant symptoms Patients with hyperparathyroidism are given large volumes of fluid in order to maintain a *dilute urine* and diminish the tendency to nephrocalcinosis and stone formation

Surgery—Removal of a *parathyroid adenoma* promptly arrests the course of the disease and is attended by rapid improvement The skeletal lesions tend to regress within a few months The blood calcium falls and the phosphorus rises but the serum phosphatase value remains elevated for a considerable period The progressive decline in renal function ceases and there may be a marked improvement

The surgical principles involved in the exploration for and removal of parathyroid adenomas are worthy of emphasis While 80 per cent of the patients with primary hyperparathyroidism have a single adenoma there are instances in which two or more adenomas are present and must be removed. Failure to find the adenoma in a patient with unequivocal clinical findings requires a thorough search for aberrant parathyroid tissue

In *primary diffuse hyperplasia* removal of three of the enlarged glands and part of the fourth has been advocated as the most rational procedure The remaining glandular tissue may subsequently hypertrophy and produce a recrudescence of the disease or it may atrophy completely with the development of *intractable hypoparathyroidism* (p 12°2)

POSTOPERATIVE COMPLICATIONS —Removal of the parathyroid adenoma is often followed by the development of *hypocalcemia* and *tetany* The first symptoms usually appear within twenty four hours after operation and consist of *paresthesias* in the fingers and toes Subsequently all the features of manifest tetany may be present in sufficient degree to prove fatal *Recalcification tetany* is due to the lime salt depletion of the skeleton in hyperparathyroidism and the huge demands of the bones for calcium and phosphorus after operation With the correction of the disease there is a rapid flow of calcium and phosphorus from the extracellular fluids to the bones with a sharp fall of blood calcium Only when the demands of the bones have been supplied from exogenous sources of supply does the blood calcium level rise to normal The blood phosphorus level remains low and may fall to lower levels As a rule this type of tetany bears some relation to the preoperative level of the blood phosphatase and is apt to be most severe in patients with high phosphatase values

The onset of tetany is forestalled by the oral administration of large amounts of *calcium chloride calcium lactate* or *calcium glyconate* (p 604)

the fecal excretions of calcium and phosphorus are increased to compensate for the impaired urinary elimination of these metabolites

Renal Function—Renal function is frequently diminished although laboratory tests may reveal only slight changes The tempo of the renal insufficiency is exceedingly slow and the functional changes are reversible

Roentgenography—Roentgenograms show varying degrees of *osteoporosis* and *metastatic calcification* The skull has an irregular finely granular appearance which is most marked in the calvarium The tables are often thickened and there may be a cotton wool appearance suggesting *Paget s disease* Rarefied cystic areas varying in size from a small pea to a large orange are seen in any of the bones and frequently expand to the cortices Large cysts are common in the heads of the humerus and femur the pelvis and the mandibles Infrequently, there is no roentgen evidence of skeletal pathology

Calcified areas are seen in the periarticular tissues the large vessels and the cortex of the kidney Staghorn renal calculi are clearly delineated and may be chance findings

Differential Diagnosis—The conditions whose clinical manifestations require differentiation from hyperparathyroidism *include* rickets multiple myeloma Paget s disease skeletal carcinomatosis senile osteoporosis and renal lithiasis

Rickets—The rare instance of hyperparathyroidism in childhood may be mistaken for the more frequent disturbance of late rickets Differentiation is based on the demonstration of metabolic evidences of hyperparathyroidism and the failure of the child to respond to the administration of calcium and vitamin D See p 620

Multiple Myeloma—Multiple myeloma may resemble chronic hyperparathyroidism due to the presence of bone pain deformities fractures hypercalcemia and renal insufficiency The chief differential points are the presence of *hyperglobulinemia Bence Jones proteinuria* and a normal serum phosphatase with the demonstration of *myeloma cells* on sternal puncture (p 1043)

Paget s Disease—Paget s disease offers no great difficulty in differential diagnosis from hyperparathyroidism Serum calcium and phosphorus values are normal while the serum phosphatase activity is increased to a very high level The roentgen picture of Paget s disease shows large circumscribed areas of rarefaction surrounded by osteosclerotic areas See p 2879

Polycystic Fibrous Dysplasia—In polycystic fibrous dysplasia the lesions are predominantly unilateral The affected bones show large scarlike areas containing grayish white fibrous tissue in the medullary cavities The disturbance occurs in childhood and early adolescence and runs a long course with considerable pain Pathologic fractures are frequent and give rise to skeletal deformities In certain severe cases encountered in young girls hyperpigmentation and precocious menstruation are seen (*Albright s syndrome*) The serum calcium phosphorus and phosphatase levels are all within normal limits and there is no negative calcium balance

Senile Osteoporosis—In senile osteoporosis there is a generalized osteo

nancy (p 2674) The hypoparathyroidism of older children may be attributed to postinfectious atrophy similar to the orchitis of mumps

Treatment—The treatment of acute postoperative tetany following thyroidectomy or the removal of parathyroid tissue requires the prompt but slow intravenous injections of 10 to 20 cc of 5 per cent *calcium chloride* or of 10 cc of 20 per cent *calcium gluconate* The latter also may be given *intramuscularly* and as relief is transient the injection must be repeated after one or two hours The calcium injections may be supplemented by oral doses of 2.5 to 5 cc of *dihydrotachysterol* (*A T 10*) or the intramuscular use of *parathyroid hormone* whose effect begins in four hours and may last for a complete day

As soon as the patient is cooperative a *high calcium intake* is provided through the use of *milk* and *aqueous solutions of the acid producing lime salts* such as *calcium chloride* using 1 gm doses up to 6 to 8 gm daily The watery preparations of calcium lactate or gluconate are more palatable but must be given in the larger doses of 10 to 12 gm daily The calcium salts are rendered less active if they are dissolved in milk hence it is wise to administer them between milk feedings Parathyroid hormone injections are discontinued as soon as is possible overdosage may produce a dangerous hypercalcemia and the preparation loses its influence after several months of use A high intake of vitamin D is assured by using daily doses of 60 to 90 drops of *viosterol* and 0 25 to 1 cc of *dihydrotachysterol*

CLINICAL DISTURBANCES OF THE PARATHYROID GLANDS

The clinical disturbances of the parathyroid glands are of significance only as they are reflected by the physiological derangements of *hyperparathyroidism* and *hypoparathyroidism* Diminution of parathyroid tissue results from *surgical ablation* (p 1216) or *fibrosis* Hyperparathyroidism is produced by *adenomas* or *glandular hyperplasia*

Adenomas—Parathyroid adenomas are more frequently observed in middle aged females who have borne several children There is a suggestion that their development may be related to the *repeated glandular stimulations* during pregnancy Furthermore since the tumors are seen with greater frequency in areas where rickets is common (Northeastern United States and the British Isles) it may be that the endocrine and metabolic factors unite to stimulate the growth of these neoplasms

The pathology chemical changes clinical manifestations and surgical treatment of *hyperparathyroidism resulting from parathyroid adenomas* appears elsewhere (p 1225)

Hyperplasia—Hyperplasia of parathyroid tissue may be obviously secondary and compensatory or apparently idiopathic The clinical implications of both varieties are discussed under the heading of *hyperparathyroidism* (p 1225) Surgical therapy of the primary type is clearly indicated when the symptoms warrant but removal of a compensatory hyperplasia can have only unfortunate results

THE CAROTID GLAND

The carotid body has the appearance of a member of the chromaffin system It contains sheets of granular and polyhedral cells and a chro

Vitamin D is supplied by three daily doses of 60 to 90 drops of *viosterol* (p 621) With the appearance of active tetany the calcium salts are given intramuscularly or intravenously and their effects are enhanced by injections of *parathyroid hormone* or oral doses of 2.5 to 5 0 cc of *dihydrotachysterol* (p 621) as in the treatment of hypocalcemia

HYPOPARATHYROIDISM

The development of hypoparathyroidism leads to the production of *tetany* The clinical manifestations of tetany are elsewhere described since they may occur from a wide variety of conditions which produce hypo calcemia The commonest of these is infantile tetany a functional disorder due to dietary deficiencies The present concern is organic *parathyroid tetany* a rare variety of the disturbance which is encountered following thyroidectomy, after the removal of a parathyroid adenoma or the resec tion of hyperplastic parathyroid tissue, or as an idiopathic condition of the newborn

See *Differential Diagnosis of Hypocalcemia* (p 724) *Differential Diagnosis of Hyperpotassemia* (p 731)

With diminution or absence of the parathyroid hormone the level of blood *calcium* falls and there is a rise in the concentration of inorganic *phosphorus* Both elements are retained in the body as evidenced by the disappearance of the ions from the urine The inability to excrete calcium is dependent upon the hypocalcemia whereas the hypophosphaturia re sults from failure of renal function

Following Thyroidectomy—Hypoparathyroidism may result from the in advertent removal or injury of one or more parathyroids during *thyroidec tomy* Occasionally it occurs after ligation of the inferior thyroid arteries after crushing injuries to the parathyroid substance with hemostats and as a result of interference with the parathyroid circulation by hemorrhage edema and scar tissue formation

The time of onset after operation depends on the *severity* and *mech anism* of the parathyroid injury With pressure edema symptoms appear within twenty four to forty eight hours after operation and reach a max imum by the fifth day The onset is usually gradual the first symptom being a sensation of pins and needles' in the finger tips When all the parathyroid tissue has been removed surgically the onset occurs in a few hours and is marked by extreme restlessness mental distress and delirium With severe initial symptoms death may be due to spasm of the *glottis* or *diaphragm* If the interference is produced by contracting scar tissue the tetany may not appear for two to three weeks and on rare occasions may come on months after operation

The course and prognosis vary with the state of residual parathyroid function and the efficacy of replacement therapy Mild instances tend to clear within three to four weeks but severe injuries require months to be come symptom free

Neonatal Tetany—On rare occasions tetany occurs in infants and chil dren in whom there is no obvious rea on for the derangements of the metabolism of calcium and phosphorus It has been suggested that neo natal tetany is related to the physiological *hyperparathyroidism of preg*

Great Britain and Ireland concluded after investigating the evidence that ther is no evidence that so-called status thymicolymphaticus has any existence as a pathological entity"

Without entering into the merits of the controversy the present section will outline the clinical manifestations of thymic asthma and status thymicolymphaticus and the pathological variations of hyperplasia and malignancy of the gland

Thymic Asthma and Status Thymicolymphaticus—Whatever their etiology and pathogenesis thymic asthma and status thymicolymphaticus present urgent and occasionally fatal consequences in clinical practice During the first three months of life otherwise healthy infants are noted to have persistent *cough cyanosis dyspnea* and attacks of *suffocation* which may progress to the convulsive stage with a termination in sudden *death*

Radiographs of the chest of these children occasionally reveal widening of the *thymus shadow* and definitive evidence of *tracheal compression*

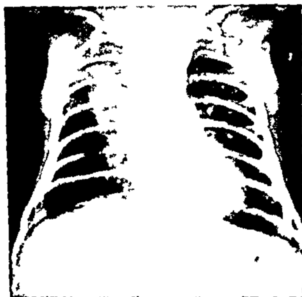


Fig 2 5—Anteroposterior view of the chest showing the dense shadow cast by the enlarged thymus on the right side of the mediastinum

The latter finding may be corroborated by bronchoscopy and postmortem examinations provide first hand evidence of mechanical compression and enlargement of the gland

Whereas many astute pediatricians believe that the enlargement of the gland is purely coincidental and unrelated to the clinical symptomatology the practitioner is wise if he insists upon routine anteroposterior and lateral roentgenograms of the chest immediately after the birth of the infant In the presence of any of the symptoms of thymic asthma or status thymicolymphaticus or a demonstrable widening of the thymic shadow one or two *prophylactic exposures to roentgen therapy* can do no harm and in the opinion of some may be life saving If this therapy is not inaugurated and the child is the victim of a sudden fatal attack it is difficult to justify what may seem to have been negligence

Bromer in Medical Clinics of North America

maffin substance Its function is not known but *chromaffinomas* occasionally are encountered with the production of the *carotid sinus syndrome* also known as the *vasovagal syncope of Lewis* (p 921)

THYMUS

Although the thymus gland is regarded by many investigators as a vestigial structure there are clinical disturbances in which the gland may have active participation

Anatomy and Physiology—The thymus gland is situated retrosternally and varies considerably in size and proportions Its weight normally should not exceed 40 gm but most often it is less than 30 gm



Fig 254—The enlarged thymus at autopsy is shown projecting downward over the base of the heart and overlapping the right lung *

The active participation of the organ in the normal economy is suggested by experimental and clinical evidence Thymectomized rats show a retardation in growth and the intraperitoneal injection of a thymus extract is said to accelerate normal growth Clinically the significance of thymic hyperplasia in the syndromes of thymic asthma and *status thymicolymphaticus* has been much debated Certainly the anatomical position of the organ suggests a possible mechanical factor in respiratory phenomena of obstruction Beyond this however enthusiastic endocrinologists have suggested a more subtle participation in pylorospasm vagotonia spasmophilia infantile tetany breath holding spells" congenital laryngeal stridor and infantile convulsions

Most of these conjectures have been summarized as good examples of the growth of medical mythology in which a nucleus of truth is buried beneath of pile of intellectual rubbish conjecture bad observations and rash generalizations (Greenwood and Wood Boyd's Surgical Pathology p 841) Th Medical Research Council and the Pathological Society of

* Bromer in Medical Clinics of North America

CHAPTER 58

THE ABDOMINAL GLANDS PANCREATIC INSULAR TISSUE ADRENAL GLANDS

THE PANCREATIC INSULAR TISSUE

The pancreatic insular tissue secretes *insulin* the specific hormone whose main function is the regulation of carbohydrate metabolism There is also the possibility that the pancreas manufactures an *insulin free substance* which may be of some significance in the lipoidal disorders as well as psoriasis (p 3414) *pancreatic lipocaic* is presently under experimental investigation

Insulin

Physiology —The functional importance of insulin is indicated by a brief consideration of the metabolic changes known to result from insulin deficiency The *blood sugar content becomes abnormally high* and if the renal threshold for glucose is exceeded *glycosuria* results The *respiratory quotient falls* from the level characteristic of normal individuals on a mixed diet and *fails to rise* in response to exercise epinephrine and glucose *The excretion of nitrogen* is increased indicating an excessive rate of protein breakdown Large quantities of gluco e are formed from protein in the liver and maintain the hyperglycemia and the glycosuria There is an

Hyperplasia of the Thymus—Hyperplasia of the thymus is demonstrable in a variety of clinical disturbances The relationship of the morphological finding to the physiological derangement is far from clear Hyperplasia occurs in *hyperthyroidism* (p 1197) *acromegaly* (p 1156) with lesions of the *adrenal cortex* (p 1266) with *myasthenia gravis* and other myopathies (p 2880) following *adrenalectomy* and following *gonadectomy*

The incidence of thymic hyperplasia is difficult of estimation since roentgenographs are rarely made for the specific delineation of the thymic shadow Except in myasthenia gravis roentgen therapy of the organ is rarely attempted since there is little reason for anticipating any therapeutic benefits

Malignant Thymoma—The malignant thymoma is the most frequent of the rare thymus tumors The neoplasm is highly invasive It compresses the trachea and other local structures spreads to the lungs and produces widespread distinct metastases

Treatment may be attempted by roentgen exposure but the prognosis is poor

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excessive combustion of fat so that fatty acids (ketones) accumulate in the blood The *ketone bodies* decrease the *alkali reserve* and with the persistent glycosuria deplete the organism of body water and fixed base There is an increased mobilization of neutral fat a rise in the fat content of blood including neutral fat cholesterol and phospholipids and the accumulation of large amounts of fat in the liver which impairs its function

Chemistry —Insulin is obtained from an alcoholic extract of beef or pig pancreas It is an amorphous powder which has been freed of foreign protein by iso electric precipitation In the presence of zinc or cadmium the hormone can be obtained in crystalline form Structurally it is a protein of high molecular weight (35 000) The molecule contains a large number of different amino acids but no chemical configuration or particular amino acid has been found to account for its activity Hydrolysis with acids or enzymes results in the complete loss of activity and for this reason insulin is ineffective when given orally

Standardization —The physiological activity of insulin is determined by measuring its ability to depress the blood sugar of fasting rabbits weighing at least 1 5 kg Preparations of the hormone are assayed by comparing their ability to lower the blood sugar of rabbits with that of U S P Zinc Insulin Crystals (Reference Standard) One unit of insulin is the amount that will lower the blood sugar of the test animal to the level of 45 mg per cent or less in five hours The potency of the standard crystalline zinc insulin is 22 international units per mg

TABLE 83 —THE INSULINS

Product	Units per cc	Remarks
Insulin Injection U.S.P	20–40–80–100	Aqueous solution rapid and transitory action
Protamine Zinc Insulin N N R	40–80	Suspension delayed and sustained reaction
Zinc Insulin Crystals N N.R	1 mg = 22 units	For standardization
Crystalline Zinc Injection N N R		As insulin injection
Globin Insulin N R R	80	Aqueous solution moderately rapid and moderately sustained reaction

Preparations —Insulin U S P is marketed as an aqueous solution in 5 or 10 cc vials containing 20 40 80 100 units per cubic centimeter In order to keep the injection mass as small as possible the 40 80 and 100 unit strengths are most widely used An insulin preparation containing 500 units per cubic centimeter may be obtained for patients requiring enormous doses of the hormone (1000 to 2000 units daily) In addition to solutions of the amorphous powder olutions of crystalline insulin are obtainable but apparently possess no advantage over regular insulin

When allergic reactions to *beef insulin occur special pork and sheep insulins* may be tried

Protamine zinc insulin N.N.R. is insulin combined with zinc and a basic protamine and is injected subcutaneously as an even suspension. The minimum solubility of the suspended particles of the compound occurs at the *pH* of the body fluids. The insoluble protamine zinc insulin is slowly broken down and the active insulin is released in small quantities over a long period simulating the secretory activity of the pancreatic islands.

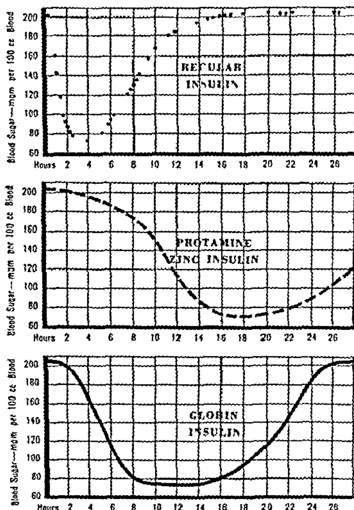


Fig. 236.—Blood sugar curves after administration of regular insulin, protamine zinc insulin and globin insulin. Note prompt and prolonged effect of globin insulin.

In the preparation of protamine zinc insulin 1 mg. of zinc is added to 500 units of insulin. The metal is relatively nontoxic and the amount administered is extremely small even during a period of years. This type of insulin is available in vials containing 40 to 80 units per cubic centimeter. To insure proper dosage before injection an even suspension must be obtained by careful shaking.

Courtesy of Burroughs Welcome & Co. Ltd.

Globin or globulin insulin with zinc is a clear almost colorless aqueous solution Each cc contains 80 units of insulin, 3 04 mg of purified globulin and 0 24 mg of zinc in the form of zinc chloride The globin is derived from the hemoglobin of sheep blood and is purified and sterilized by filtration methods before addition to the other sterile ingredients of the preparation As an added safeguard to sterility 0 18 per cent cresol is added, the *p*H of the final product is about 7 3 Globin insulin is stable and no noticeable change in potency or duration of action has been found after storage in a refrigerator for more than two years

The action of globin insulin is both prompt and prolonged It is not so rapid in its effects as regular insulin and not so prolonged as protamine insulin The hypoglycemic effect is generally apparent within two hours after subcutaneous administration the period of greatest activity extends from the eighth to the sixteenth hour after injection At the end of twenty four hours when the time for the next daily injection arrives the blood sugar level approaches normal

Globin insulin has advantages over regular and protamine products The regular insulin produces its effect with too great rapidity and the duration of the hypoglycemia is much too transitory for therapeutic effectiveness Protamine zinc insulin may produce local allergic cutaneous manifestations It is a suspension and it is necessary to mix it thoroughly before injection The onset of action is slow so that it may be necessary to give a simultaneous dose of regular insulin Its prolonged activity may lead to hypoglycemic reactions during the night

Mode of Administration —Since insulin is destroyed in the gastro intestinal tract it must be given parenterally usually by the *subcutaneous route*

In diabetic emergencies (coma) *intravenous administration* is used When given by vein the onset of action is immediate but the maximal effect is short lived since the hormone is rapidly destroyed and excreted

After *subcutaneous injection* the peak effect is obtained in from one to three hours The site of injection should be changed frequently so that not more than one injection is given in the same spot Frequent injections in the same area lead to poor absorption and nullify the effect It has been recommended that users of insulin construct an insulin map of the body on which the points of insertion of the needle for a month can be recorded The superficial layers of the skin should be avoided since insulin so injected may give rise to insulin burns or blisters

Therapeutics —The administration of insulin promptly lowers the blood sugar of the diabetic It increases the oxygen consumption and raises the respiratory quotient It increases the glycogen content of the liver and muscles and reestablishes carbohydrate metabolism This depresses the excessive production of fatty acids

The action of insulin is not entirely understood and is certainly not a simple one It apparently takes part in some phase of cellular metabolism enhancing the cellular utilization of carbohydrate and *regulating its production* from noncarbohydrate sources (chiefly protein) Since the diabetic organism can still burn sugar the relative importance of impaired glucose utilization and of the overproduction of glucose in the pathogenesis of diabetes remains to be determined

The problem of insulin action is further complicated by the many factors that affect the sensitivity to the hormone Insulin action is interfered with by antagonistic hormones i e epinephrine thyroxin posterior pituitary extract the diabetogenic factor of the anterior pituitary and probably certain of the adrenal cortical steroids (corticosterone) A change in the acid base balance toward the acid side renders insulin less effective The products of infection or the inflammatory process itself decrease sensitivity to insulin by interfering with its action or by increasing the rate of glyconeogenesis from protein It has been suggested that a hepatic enzyme is essential for the normal action of insulin and that any reduction in the supply of this ferment (insulin kinase) makes the organism less responsive to insulin It is also possible that the blood may contain at times an enzyme system which is capable of inactivating insulin

On the other hand the sensitivity of a diabetic to insulin is known to increase With good treatment there may be improvement to the point where exogenous insulin need no longer be administered The value of a standard quantity is often enhanced by exercise weight reduction a high carbohydrate low fat diet zinc and large doses of sodium chloride

Insulin in Diabetes Mellitus—The chief use of insulin is in the treatment of diabetes mellitus A detailed discussion of this disease and of the management of diabetic patients will be found elsewhere (p 1246)

Insulin in Nondiabetics—Patients who suffer from malnutrition or chronic wasting disease associated with anorexia may receive insulin in doses of 5 to 10 units before the principal meal in order to stimulate appetite by the production of a mild hypoglycemia This procedure is of particular value in the visceroptotic in health and in patients who suffer from pulmonary tuberculosis

Untoward Reactions to Insulin—Hypoglycemic shock insulin allergy and local irritation are hazards of insulin therapy

Hypoglycemia—A decrease in blood sugar begins to develop within a few minutes after the injection of insulin Lack of an adequate food supply particularly carbohydrate either in the diet or as a reserve stored in the body favors a depression of the blood sugar below normal levels

The symptoms of hypoglycemia are extreme hunger accompanied by a feeling of faintness muscle weakness sweating and vomiting A variety of central nervous system manifestations may appear i e inability to speak double vision mono and hemiplegia involuntary micturition or defecation hallucinations somnolence and unconsciousness With protamine zinc insulin the symptoms come on more slowly are less severe and are more easily recognized by the patient However the insidious nature of these reactions is a danger The patient may slowly drift into unconsciousness without premonitory symptoms

The *prognosis* in insulin reactions is good There are usually no sequels even though the symptoms have been severe In a group of elderly patients with coronary arteriosclerosis hypoglycemic reactions are dangerous and may precipitate cardiac pain or an acute coronary occlusion

Within a few minutes 5 to 10 gm of glucose orally usually relieve a patient suffering from hypoglycemia The longer the period of an insulin reaction the more carbohydrate is required As much as 200 gm of glucose may have to be given before the blood sugar starts to rise If glucose can

not be ingested (vomiting or coma) an injection of 1 cc of a 1 1000 solution of epinephrine will raise the blood sugar level promptly but transiently

Insulin Allergy—Any of the forms of insulin may produce *allergic phenomena* The reaction may take the form of a local tender red swelling about the site of an injection These occur with each injection but tend to disappear after a few weeks Less commonly, a general urticarial reaction may be observed and may be attended by fever and extreme insulin resistance Such cases may be desensitized by intradermal injections of insulin beginning with 0 001 unit

Local Reactions—Repeated injections of insulin into the same site often lead to necrosis of the subcutaneous tissue and the production of lumps Such areas are susceptible to infection Localized lipomatosis has been observed at the site of insulin injections

Areas of lipodystrophy in which there are depressions of the surface of the skin with almost complete disappearance of subcutaneous fat occur at the sites of insulin administration The cause of such atrophies is unknown

Clinical Disorders of Pancreatic Insular Tissue

The functional disturbances of the insular tissue of the pancreas are in the nature of the uncommon episodes of *hyperinsulinism* and the exceedingly frequent manifestations of *hypoinsulinism* most often related to *diabetes mellitus*

HYPERINSULINISM

Hyperinsulinism is caused by the overproduction of insulin by the islet tissues of the pancreas For the most part the clinical manifestations are due to *hypoglycemia* and are similar to those observed after an overdose of *insulin*

Etiology —Organic hyperinsulinism in the adult may result from insulin producing tumors of the islets or hypertrophy hyperplasia and functional hyperactivity of normal appearing islet tissue *Benign adenomas* are the most commonly encountered tumors and are the predominant cause of the disorder They are amenable to surgical extirpation which produces a dramatic cure *Hypertrophy of the islets* without tumor formation has been observed in a few patients and successfully treated by subtotal pancreatectomy Functional hyperinsulinism is not well established as a clinical entity In disorders of this type the production of insulin is not excessive but there may be a disturbance of the mechanism which regulates the release of insulin in response to the demands of carbohydrate metabolism

Hyperinsulinism also occurs *in infants born of diabetic mothers* These children are subject to hypoglycemic episodes during the first few days of life The neonatal hyperinsulinism is a compensatory phenomenon in response to the maternal insulin deficiency and is happily temporary

Pathology —The pathology of hyperinsulinism is observed in the pancreas and in extra pancreatic areas

Adenomas —Adenomas of the islands of Langerhans are well demarcated, reddish growths varying from 4 mm to 2 cm in diameter When superficially located, they stand out on

the surface of the gland as *lilac colored nodules* but they may be buried in pancreatic tissue The tumors are most frequently encountered in the *tail of the pancreas* but have been found in all parts of the gland As a rule there is only one growth but there are in stances in which two and four adenomas have been present

Microscopically the tumors are gigantic islands of Langerhans There is an exact dupl cation of the pattern of the normal islets with a rich capillary network bordered by rows of cuboidal and columnar cells The tumor cells are similar in size to normal islet cells and contain fine granules with similar staining reactions As in normal tissue there is often ex tensive fibrosis hyaline degeneration and calcification of the islets The latter changes are particularly apparent in larger tumors The tumors are believed to arise from the epithel um of the pancreatic ducts and have been termed *nesidioblastomas*

Carcinomas—Carcinomas of the islet cells are small Metastases occur to the regional lymph nodes and the liver The cells resemble normal islet tissue but are arranged in rosettes around capillaries in sheets and in tubular and ribbon formation Fibrosis hyal ne degenera t on and calcification may be extensive

Hypertrophies—In the rare hypertrophies the islet may be increased 50 per cent above normal in size The cells are enlarged and there is evidence of hyperplasia but no tumor formation The islands are normal on pathological examination in *functional hyperinsulinism*

Extrapancreatic Lesions—The extrapancreatic lesions are meager and are almost entirely limited to the central nervous system *Cerebral edema* and perivascular infiltrations may be encountered after frequent convulsive seizures There may be mult ple punctate *cereb al hemorrhages* acute degeneration of the cerebral neurons and advanced destruction of the cerebral cortex thalamus and corpus striatum The histological findings are analogous to those seen in primary degenerative d seases of the nervous system and in encephalopathies due to exogenous toxins Acute swelling of the neurons paling of the tissue, degeneration and secondary glial prol ferations are obs rved The *l ver* is usually normal in appearance and in glycogen content but fatty infiltration and glycogen depletion have been seen

Clinical Manifestations—Organic hyperinsulinism is a rare disorder which occurs with equal frequency in the sexes and is most common during the third and fourth decades The clinical manifestations are the result of the acute episodes of hypoglycemia

Acute Hypoglycemic Episodes—The patient with hyperinsulinism suf fers from recurring seizures These are identical with those produced by an overdose of insulin There is usually an *aura* of weakness trembling anxiety sweating and hunger followed by mental confusion and any of a great variety of *psychiatric disturbances* including disorientation nega tivism mania confabulation hallucinations delusions and amnesia The patent may lapse into coma or may experience generalized epileptiform convulsions Many patients are regarded initially as *epileptics* or *brain tumor suspects* The severity of the symptoms and the depth of the coma are not closely related to the degree of hypoglycemia

Although the seizures are by no means typical and simply indicate the existence of a hypoglycemic state there are a number of findings that are suggestive of hyperinsulinism The majority of patients note a relationship of the attacks to *hunger* and *physical exertion* and report prompt relief on taking food The appetite is usually excessive and there is a strong desire to eat between meals Many patients develop a craving for sweets of all kinds and periodically engage in a sweet spree which tends to aggravate the disorder Others drink large amounts of sweetened coffee and other caffeine containing beverages Most patients learn to recognize the premonitory symptoms of an attack and prevent its further develop ment by eating However should the victim oversleep miss a meal or en gage in strenuous exercise an attack is likely to occur Occasionally the attack occurs at the sight of food or several hours after a hearty meal

Phases of extreme sensitiveness to exercise fasting diarrhea loss of weight, and menstruation which provoke hypoglycemic reactions are recognized Alternating with these are long intervals in which it is difficult to elicit an episode The increased sensitiveness is especially pronounced in females during menstruation On the other hand the attacks are less frequent and milder during acute infections

Abdominal discomfort and *epigastric tenderness* may be prominent features of the clinical picture These complaints usually come on several hours after meals when the stomach is empty They are relieved by food and simulate the symptom complex of *peptic ulcer*

Overindulgence in carbohydrate foods which is an almost constant response of these patients to recurrent hypoglycemia leads to the development of *obesity* The typical patient is 50 or 75 pounds overweight and gives a history of a fairly rapid weight gain shortly after the onset of the disorder In occasional instances the episodic character of the *neuropsychiatric manifestations* is supplanted by permanent mental and neurological findings which are not relieved by treatment

The onset is usually gradual with mild symptoms for long periods Many patients learn to temper the disorder by the maintenance of over nutrition and by taking frequent small feedings In some patients there may be an abrupt onset of severe attacks attended by *convulsions* and *coma* This is especially apt to occur in patients with carcinoma of the islets which is the most marked form of hyperinsulinism In patients with adenoma the attacks are milder and the disorder may remain static except for the phase like variations in the intensity and frequency of the attacks

Laboratory Findings—The *fasting blood sugar* is low Values of 35 to 60 mg per cent are usually encountered Withholding food for several hours after the usual breakfast time further depresses the blood glucose level and may bring on a hypoglycemic seizure Some patients tolerate fairly low blood sugar levels with a few clinical manifestations while others are intolerant of only a slight depression below the normal Three to four hours after a meal the blood sugar may be lower than the fasting value obtained before breakfast This phenomenon which is typical of organic hyperinsulinism is due to the excessive liberation of insulin by the stimulus of food and has been termed stimulative hypoglycemia which is an exaggeration of a normal response

There is considerable variation in the shape of *dextrose tolerance curves* A low flat curve is usually obtained but there may be a high plateau curve of the diabetic type These variations are due to differences in the dietary habits of individual patients A high carbohydrate diet increases the glucose tolerance and is associated with a flat curve while a diet poor in carbohydrate decreases tolerance and tends to give a delayed hypoglycemic response The use of a standardized diet for several days prior to the performance of a glucose tolerance test makes for greater uniformity in the shape of the curve which is typically flattened *A six hour test* is recommended since the curve may be normal during the first three hours and becomes hypoglycemic only when the period of observation is prolonged

Differential Diagnosis —Organic hyperinsulinism must be differentiated from the spontaneous hypoglycemias (p 734) disorders of the central nervous system epilepsy and the psychoses

The principal features of hyperinsulinism include periodic transitory episodes of a neurologic or psychiatric nature apparent absence of the usual neurologic and psychiatric causes relation of attacks to hunger and exertion tendency to gain weight well being between attacks hypoglycemia and prompt relief from the administration of dextrose

See *Differential Diagnosis of Hypoglycemia* (p 734)

Treatment —The treatment of hyperinsulinism consists of measures directed at the relief of the acute hypoglycemic seizures the prevention of these episodes by dietary measures and removal of the underlying cause of the condition whenever possible

Treatment of Acute Hypoglycemic Episodes —The acute hypoglycemic episodes respond promptly to parenteral and oral *dextrose* As in insulin shock (p 1241) injections of *epinephrine hydrochloride* (0 5 to 1 cc of a 1 1000 solution subcutaneously) are a valuable adjunct since the hyperglycemia produced in this fashion is not apt to stimulate a recurrence of hypoglycemia

Prevention of Hypoglycemic Episodes —Many patients are satisfactorily controlled for long periods by the institution of a proper dietary regimen A *low carbohydrate diet* containing liberal quantities of fat and given in frequent small feedings is tolerated best Harris advises a carefully calculated diet to meet the nutritional needs of each individual patient The average patient requires about 2250 calories obtained from 90 to 150 gm of carbohydrate 60 to 75 gm of protein and the remainder from fat largely cream and butter The food is taken in five to seven small feedings

Obese patients are given a low caloric diet with feedings every two hours A caloric value of 1260 calories is obtained from 120 carbohydrate 60 protein and 60 fat *Asthenic patients* are given 90 to 150 carbohydrate 60 to 75 protein and 200 to 300 fat A high protein diet of 120 to 140 gm is advocated by some physicians since the glucose derived from protein is liberated slowly and does not stimulate the production of insulin Carbohydrate is provided best in slowly absorbed forms such as 3 10 or 15 per cent fruits and vegetables bread and cereals

Drugs with the exception of epinephrine hydrochloride in the acute attacks are of limited value *Phenobarbital in doses of 30 0 mg (½ gr)* in the morning at night and after meals is helpful Psychotherapy has its advocates in functional types of hyperinsulinism

Surgical Treatment —Surgery is indicated when attempts to control the disorder by diet are ineffective and when a benign adenoma or a carcinoma is suspected *An exploratory laparotomy is considered under the following circumstances*

1 With acute fulminating episodes which are refractory to therapy
2 In chronic disturbances that cannot be controlled by diet
3 With severe neuropsychiatric symptoms of long duration

The search for a tumor must be thorough If the disease persists after the removal of one tumor a second exploration is indicated for additional

growths If the tumor cannot be palpated partial resection of the pancreas is performed A transitory hyperglycemia following operation is regarded as a favorable sign

DIABETES MELLITUS

Diabetes mellitus is a disorder of *carbohydrate metabolism* in which there is an elevation of the sugar content of the blood loss of glucose in the urine an excessive catabolism of protein and fat and an increased loss of body water and electrolytes It is classified for present purposes as a hypo insulinemia though there is much evidence to suggest that other disturbed mechanisms in the liver adrenal cortex and anterior pituitary glands are prime operative causes

Incidence —Diabetes is the most common of the recognized disorders of the endocrine system Over 30 000 Americans died with the disease during 1937 more than a half million suffer from diabetes at the present time and probably two and a half million more of the present population sooner or later will develop the disease Diabetes occurs at all ages but the commonest age of onset is after forty five About 5 per cent of the patients are in the first decade of life with a steady increase to 24 per cent during the fifth and sixth decades The peaks of onset are puberty and the menopause during periods of intense glandular upheaval Up to the age of forty both sexes are equally affected. After forty the incidence among females increases especially in women who have borne children

Etiology —Many factors contribute to the genesis of diabetes which is obviously appearing in increased incidence under the stress of modern civilization

Heredity —Genetic studies indicate that diabetes is inherited as a *mendelian recessive* The disease is not uncommon among identical twins and there is a greater incidence in the relatives of diabetics than in those of nondiabetics

Obesity —The tendency to obesity is found in the majority of adult diabetics and there is an increased incidence of the disease at times when there are great gains in body weight The adult mortality rate increases with the degree of obesity Conversely weight reduction usually produces amelioration of the disease and often results in its arrest Obesity has been regarded as an exciting factor which brings out an inherited predisposition to diabetes but both conditions may be the result of a single underlying endocrine disorder

Environment —Many regard diabetes mellitus as a disease of modern life and attribute it to the increased incidence to hyperalimentation sedentary physical habits and excessive mental and emotional stresses

Pathogenesis —The nature of the metabolic defect in diabetes mellitus remains obscure The obvious explanation of a simple hypo-insulinemia has many weaknesses although this condition prevails in demonstrable pancreatic diabetes Under other circumstances hepatic, adrenal cortical and anterior pituitary factors appear important, if not fundamental

The abnormality may result from *underutilization* of sugar or *overproduction* of glucose from protein and probably from fat Best states that "it is preferable to consider that both mechanisms may play a part in the production of the diabetic condition and to concentrate attention on the development of quantitative methods by which accurately to determine the extent of overproduction or underutilization"

Pancreatic Diabetes —Diabetes mellitus is reproduced experimentally by *removal of the pancreas* and by administration of alloxan which possesses the specific property of destroying the beta cells of the islands of Langerhans In human diabetics the affliction occasionally is of demonstrable organic pancreatic origin Diabetes has been observed in patients with acute and chronic pancreatitis in pancreatic lithiasis and after subtotal removal of the pancreas for hyperinsulinism or carcinoma

Hepatic Diabetes —The liver is essential to the maintenance of the diabetic state Hep-

atectomy produces hypoglycemia in diabetic animals and liver disease may decrease the severity of human diabetes Normally the liver maintains the blood sugar at a constant level by removing any excess of glycogen and by liberating sugar into the blood as needed Hyperglycemia results from factors which lead to overproduction of glucose by the liver cells or which interfere with the capacity of the organ to store glucose as glycogen Diabetes mellitus is encountered in patients with *hematochromatosis* (p 1976) in whom there is an advanced degree of hepatic cirrhosis as well as pancreatic fibrosis

It has been suggested that the functional state of the liver influences the activity of insulin by the production of an *insulin kinase* This enzyme enables insulin to act and is lacking in liver disease

Pituitary Diabetes—The pituitary gland is the source of a *diabetogenic principle* and a *trophic hormone* responsible for the normal activity of islet tissue The diabetogenic action of pituitary extracts is striking in the pancreatectomized animal If the factor is administered for several weeks to an animal previously maintained on a high carbohydrate diet, a state of permanent diabetes may be induced Conversely removal of the anterior lobe of the pituitary produces hypoglycemia an increased sensitivity to insulin and an amelioration of the diabetes of pancreatectomized animals According to Houssay the diabetogenic substance present in hypophyseal extracts acts in large part, by stimulating glycogenesis in the liver since it has little effect if any in the liverless preparation

Experimental data have strengthened the belief that *diabetes mellitus* may be of pituitary origin Hyperpituitarism is suggested by the overgrowth which occurs in 90 per cent of diabetic children prior to the onset of the disease and by the high incidence of diabetes mellitus in patients with acromegaly

Adrenal Cortical Diabetes—Removal of the adrenal cortex produces hypoglycemia an increase in insulin sensitivity in normal animals and an amelioration of the diabetes of pancreatectomized animals Adrenal insufficiency impairs the conversion of protein and fat into glucose and the administration of adrenal cortical steroids (corticosterone) corrects these defects and when given to normal animals in excess may lead to hyperglycemia

The possibility that cortical hyperfunction is involved in some instances of diabetes mellitus is suggested by the occurrence of hyperglycemia and glycosuria in the *adrenal genital syndrome* In this condition there is evidence of an increased production of adrenal steroids and metabolic studies reveal an excessive conversion of protein into carbohydrate

Thyroidal Diabetes—The thyroid hormone affects the cellular utilization of the sources of energy Hyperthyroidism which decreases sugar tolerance and sensitivity to insulin renders a diabetes more severe and more difficult to control whereas removal of the thyroid alleviates the severity of the diabetes Apparently an excess of thyroid hormone acts as a secondary factor imposing an additional metabolic strain on the prediabetic or mildly diabetic individual

Neurogenic Diabetes—Pathologic processes involving the *hypothalamus* may produce hyperglycemia and glycosuria The occasional occurrence of diabetes mellitus after acute nervous shock or after head injuries may be the clinical counterparts of the glycosurias observed after puncture of the fourth ventricle and hypothalamus in experimental animals

Pathologic Physiology—The disturbance of the sugar regulating mechanism results in *hyperglycemia* When the blood concentration of sugar exceeds the renal threshold value of approximately 160 mg per cent *glycosuria* results The extent of glycosuria depends on the carbohydrate content of the diet and the severity of the disease The *respiratory quotient* (*R Q*) falls from the normal level and fails to rise in response to exercise epinephrine and glucose The excretion of *nitrogen* is increased indicating excessive protein breakdown

The metabolism of fat is disturbed as is evidenced by the *hyperlipemia hypercholesterinemia* and the excessive production of *fatty acids* In severe diabetes there is an excessive combustion of fat with the formation of large quantities of *aceto acetic acid* and *beta hydroxybutyric acid* These products are normal intermediates in fat metabolism but because of the excessive amounts cannot be catabolized to completion They are excreted in the urine in combination with ammonia or fixed base In the bladder and in the lungs aceto-acetic acid is oxidized to *acetone*

Alterations in *electrolyte balance* are produced by the glycosuria and the production of ketone bodies If the disease is sufficiently severe to allow the urinary excretion of 120 gm of glucose there is a great loss of fluid due to the depletion of endogenous glycogen stores and the osmotic effects of the urinary glucose These metabolic defects cause a loss of *sodium* and *potassium* from the tissues and to a less extent from the blood

When ketones are produced they are first *excreted* in combination with ammonia As the ammonia forming capacity of the kidney is exceeded the *fixed base* of the body is withdrawn The salt loss is attended by water loss to preserve the isotonicity of the body fluids and extreme tissue dehydration may be encountered

Clinical Manifestations —The onset of diabetes is distinctly variable In young children and following acute infectious diseases the metabolic disorder begins abruptly with an almost explosive violence In middle aged and elderly patients the disturbance is often asymptomatic for long periods of time and may be revealed only as a chance finding in the course of a routine urine examination (*diabetes decipiens*)

The symptoms of diabetes are characteristic and usually uniform They consist of *polydipsia polyuria bulimia* and *pruritus* which almost invariably is localized to the female genitals The insatiable *thirst* is often attended by a sensation of *oral burning* The increased appetite has a paradoxical association with a *progressive loss of weight and strength* Those who were previously obese show the greatest evidences of weight loss Less frequent initial complaints are somnolence constipation dimness of vision impotence muscle pains a pyoderma or a gangrenous ulceration

Dermatoses—Skin manifestations occur with regularity in uncontrolled *diabetics* Superficial *dermatophytoses* are apt to be troublesome and often lead to serious complications due to secondary infection The skin is often dry and scaly particularly if there is dehydration and an associated *avitaminosis* *Cutaneous lipoid deposits* such as the xanthoma diabeticorum are seen about the eyelids The palms and soles may be yellow due to the high carotene content of the plasma Pyodermas such as *furunculosis* and *carbuncles* have serious implication

Digestive Disturbances—Enlargement of the liver usually the result of *fatty infiltration* is encountered most often in young children The viscus may be huge so that the abdomen is protuberant a finding of evil prognosis since it signifies a severe diabetes in which insulin reactions and episodes of acidosis are commonly encountered

The intercurrent development of acute hepatitis cirrhosis of the liver or hemochromatosis increases the severity of the diabetes and favors the development of an acidosis Tremendous doses of insulin are necessary to control the disease in the presence of these complications

Cholelithiasis (p 1997) occurs with unusual frequency in diabetics who often complain of post prandial epigastric distress intermittent pains in the right upper quadrant and recurrent attacks of jaundice In these situations there is the possibility that the gallstones served as the initial lesion and that secondarily the chronic cholecystitis and pancreatitis were instrumental in the genesis of the insular deficiency

Neurological Disturbances—The neurological disturbances that are associated with uncontrolled diabetes mellitus are now recognized as more likely manifestations of *vitamin B deficiency* They include *neuralgias paresthesias* and *anesthesias* Occasionally a *peripheral neuritis* is demonstrable and degenerative lesions of the cord produce a diabetic *pseudotabes* The peripheral neuropathy of diabetes is usually bilateral and symmetrical It involves the lower extremities first and predominantly and rarely is reflected in the arms The usual complaint is a bilateral plantar hyperesthesia of sock' distribution Often there is tenderness of the calf

muscles loss of the senses of vibration and position with absent ankle and knee jerks

Vascular Changes—The frequently encountered manifestations of cardiovascular disease in uncontrolled diabetics include *coronary sclerosis coronary occlusion cerebral arteriosclerosis* and *peripheral endarteritis* and *gangrene* The vascular changes are attributed to the disordered fat metabolism and the hypercholesteremia which is a factor of great importance in experimental atherosclerosis

Coronary occlusion (p 983) occurs twice as frequently in the uncontrolled diabetic as in the nondiabetic Acute coronary occlusion may be mistaken for diabetic coma A sudden hypoglycemia may produce angina pectoris and precipitate an acute cardiac decompensation *Arterial hypertension* is common in uncontrolled diabetes and contributes to the extent of the arterial change

Ocular Changes—Disturbances of the visual apparatus are serious and common features of uncontrolled diabetes Juvenile *cataracts* are frequent and an *iritis* may be a *presenting finding* Middle aged diabetics show a severe grade of *retinal arteriosclerosis* with deposits of hard yellowish refractile lipoid substance arranged in stellate figures in the macular regions Additionally there may be many small circular and linear hemorrhages seen in this area producing the so-called *central punctate retinitis* In severe diabetes the lipoid laden blood produces a peculiarly whitish waxy column on the retinal vessels (*lipemia retinalis*) *Optic atrophy* and *paralysis of accommodation* may be encountered and *decrease of visual acuity* is often a serious complaint

Renal Changes—Diabetics occasionally have a *massive albuminuria* resulting in *hypoproteinemia* and a *generalized edema* of the *nephrotic type* (p 2389) Pathological examination of the kidneys in this disorder shows a distinctive hyalinization of the glomerular capillaries constituting an *inter capillary glomerulosclerosis* (p 2372)

Laboratory Findings—Diabetes mellitus is essentially a laboratory disease *Glycosuria* is the most important diagnostic finding Sugar appears in the urine when the hyperglycemia exceeds the threshold value of 160 to 180 mg per cent In a mild diabetes the glycosuria is often intermittent so that a twenty four hour specimen must be examined It is a clinical axiom that glycosuria should be considered diabetic in origin until proved otherwise Nevertheless there are many substances which produce *pseudoreductions* in the urine (p 3675) and many other causes for glycosuria elsewhere discussed in greater detail (p 3673)

The degree of glycosuria parallels the severity of the disease if the dietary routine is kept at a constant In mild examples the twenty four hour urine sample contains up to 1 per cent dextrose whereas in the severer disturbances it may contain as much as 8 per cent

As the concentration of urinary sugar approaches 4 per cent *polyuria* is observed The polyuria is associated with a *high specific gravity* due to the extent of the sugar content In older diabetics with an elevated renal threshold for dextrose hyperglycemia may exist without glycosuria

The presence of *diacetic acid* and *acetone* in the urine is evidence of a ketotic acidosis and heralds impending coma *Albuminuria* occasionally is found and may be sufficiently severe to produce the diabetic nephrosis

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The initial examination of the blood in a suspected diabetic must include *fasting levels* and *curves* obtained after the ingestion of a standard sugar meal Usually the fasting blood sugar level is elevated beyond the normal figures of 120 to 150 mg per 100 cc and most often it exceed 200 mg per 100 cc Should the blood sugar figures be questionable a meal of 100 gm of dextrose in 300 to 400 cc of water is given The blood sugar levels are determined at 30 minute intervals for three hours Urine specimens are collected with blood sugar determination Under the conditions of the test there should not be a glycosuria and the fasting level of blood sugar is resumed within 1 or 2 hours In the diabetic the rise in the sugar content of the blood is excessive and the concentrations remain elevated with the appearance of a glycosuria

A variation of the classical *sugar tolerance test* has been introduced by Exton Rose For their procedure the fasting blood sugar is determined and 50 gm of glucose are administered orally At the end of a half hour another blood sugar level is determined and the second meal of 50 gm of dextrose is administered The third blood sugar is taken at the end of another half hour Using this technic it has been found that 95 per cent of diabetics have a blood sugar value of over 160 mg per 100 cc at the end of the first hour

See *Differential Diagnosis of Hyperglycemia* (p 733)

Most diabetics in addition to the hyperglycemia have a *lipemia* The rise includes increased amounts of neutral fat and cholesterol In severe diabetics the lipemia may be so extreme as to produce a milky appearance in the plasma The level of the *blood cholesterol* is so significant that many regard it as the best index of the severity of the disease Values over 400 mg per 100 cc are seen in juvenile diabetics and those whose metabolic disorder is complicated by arteriosclerosis gangrene xanthomatosis and cataracts The lipemia is apt to be associated with an elevation of the carotene content of the blood The pigments impart a yellow tinge to the skin most apparent on the palms At times the color may be sufficiently marked to suggest a jaundice The absence of a scleral discoloration in patients with carotenemia suggests the clinical differentiation The carotenemia probably represents a reduction in the capacity of the liver to convert this substance into *vitamin A* and may account also for the *avitaminosis* that is observed clinically

See *Differential Diagnosis of Hypercholesterinemia* (p 736)

Complications—It is the modern opinion that the only true complication of diabetes mellitus is the state of acidosis According to older views there was a direct relationship between diabetes and arteriosclerosis pyoderms cholelithiasis ophthalmologic disorders and the neuropathies There seemed an increased incidence of pulmonary tuberculosis The coincidental presence of diabetes and these alleged complications in many instances is the chance association of frequently encountered clinical manifestations In the remainder dietary deficiencies and the states of malnutrition engendered by a poorly controlled disturbance of sugar metabolism invited the secondary affliction

The importance of stressing these points pertains to prognosis The well controlled diabetic need dread the development of these additional burdens no more than the nondiabetic

Diabetic Acidosis—Diabetic acidosis is still a common cause for death despite the efficacy of insulin Most often the condition arises from diet ary indiscretions omission of the insulin dose the presence of an inter current infection a surgical procedure endocrine imbalance or diseases of the liver

See *Differential Diagnosis of Acidosis* (p 721)

Acidosis may supervene rapidly in any diabetic and lead to *immediate coma* It may be the first indication of an unrecognized diabetes mellitus The onset is usually gradual and is preceded by several days of dyspepsia irritability muscle pains and restlessness The patient gradually becomes disinterested drowsy and somewhat irrational The respirations are long deep and rapid (*Kussmaul breathing*) but there is no subjective feeling of air hunger as in dyspnea The breath has an *acetone odor* which may be instantly apparent on entering the sick room *The pulse is* rapid the skin dry and the pupils dilated The drowsiness leads to stupor from which the patient can be aroused but finally coma supervenes

The patient in diabetic coma is usually flushed hot and dehydrated with tachycardia and a low blood pressure The eyeballs are soft and dent easily on pressure The *urine* contains large amounts of sugar and acetone During treatment glycosuria may disappear *before* the acetonuria Less often ketones disappear or fail to appear in the urine even though still present in the blood as a result of a renal block The *blood sugar* usually exceeds 400 mg per cent but may be only moderately elevated *The carbon dioxide capacity of the blood* may be as low as 10 per cent due to reduction in the reserve alkali content of the body fluids The blood *non protein nitrogen* rises especially when the blood pressure is low and dehydration is severe The *hemoglobin* and *cell volumes* are high due to hemoconcentration There is an appreciable *leukocytosis* usually in the vicinity of 25 000 white blood cells with a polynucleosis and a shift to the left A leukemoid reaction resembling myeloid leukemia may be seen

The syndrome of diabetic acidosis may resemble other acute disturbances The patient *with nausea vomiting abdominal pain elevated temperature* and leukocytosis may appear to have an acute intra abdominal surgical emergency and differentiation from acute appendicitis is often difficult Diabetic acidosis may resemble an *acute coronary thrombosis* when patients have ill defined upper abdominal pain nausea vomiting hypotension fever and leukocytosis

Diagnosis—Diabetes mellitus is a laboratory diagnosis The practitioner is required to note the glycosuria identify the sugar on at least one examination and demonstrate a hyperglycemia

Treatment

The satisfactory management of the diabetic patient by his practitioner requires that the metabolic derangement be controlled by measures that are simple of execution *and within the range of the potentialities of the* cooperative person of normal intelligence

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Most diabetics in addition to the hyperglycemia have a *lipemia* The rise includes increased amounts of neutral fat and cholesterol In severe diabetics the lipemia may be so extreme as to produce a milky appearance in the plasma The level of the *blood cholesterol* is so significant that many regard it as the best index of the severity of the disease Values over 400 mg per 100 cc are seen in juvenile diabetics and those whose metabolic disorder is complicated by arteriosclerosis gangrene xanthomatosis and cataracts The lipemia is apt to be associated with an elevation of the carotene content of the blood The pigments impart a yellow tinge to the skin most apparent on the palms At times the color may be sufficiently marked to suggest a jaundice The absence of a scleral discoloration in patients with carotenemia suggests the clinical differentiation The carotenemia probably represents a reduction in the capacity of the liver to convert this substance into *vitamin A* and may account also for the *avitaminosis* that is observed clinically

See *Differential Diagnosis of Hypercholesterinemia* (p 736)

Complications—It is the modern opinion that the only true complication of diabetes mellitus is the state of acidosis According to older views there was a direct relationship between diabetes and arteriosclerosis pyoderms cholelithiasis ophthalmologic disorders and the neuropathies There seemed an increased incidence of pulmonary tuberculosis The coincidental presence of diabetes and these alleged complications in many instances is the chance association of frequently encountered clinical manifestations In the remainder dietary deficiencies and the states of malnutrition engendered by a poorly controlled disturbance of sugar metabolism invited the secondary affliction

2 Neither the degree of glycosuria nor the value for the blood sugar furnishes adequate criteria for the regulation of diabetes
3 The patient who oxidizes and stores the quantity of carbohydrate essential for his particular needs approaches the normal state whether or not he has sugar in his urine
4 The administration of sufficient protamine insulin to insure the utilization of the optimum of carbohydrate restores and maintains a metabolic state that approaches the normal
5 Patients treated with protamine insulin according to these tenets are rendered socially and economically useful despite the constant glycosuria
6 The glycosuric patients do not develop more frequent nor more severe infections When surgical measures are required their wounds heal as readily as those of patients whose urines were sugar free
7 The protamine-regulated glycosuric patients report extreme well being and maintenance of an optimum weight They are not in the constant jeopardy of a hypoglycemic reaction from an overdose of insulin as are other diabetics whose urines are kept free from sugar
8 The persistent glycosuria does not produce polyuria frequency of urination and polydipsia, provided that weight is maintained and ketosis and diabetic symptoms are controlled
9 The protamine glycosuric patients do not have a tendency to develop ketosis so long as there is maintenance of weight and freedom from diabetic symptoms
10 The continuous and constant glycosuria is compatible with nitrogen equilibrium
11 Vascular sclerosis apparently is not dependent upon hyperglycemia and does not occur more readily or more extensively in the controlled glycosuric patient

Laboratory Controls for the Management of Diabetes—The laboratory controls for the management of diabetes in private practice must be simplified to the point where they can be performed with facility by the physician and his patient These essentials are noted in Table 84

The Basic Diet—In the section on Dietotherapy a basic American diet for the person of average weight and height has been outlined (p 608) At rest such a subject weighing in the neighborhood of 150 pounds without *performing arduous labor or exercise requires approximately 1500 calories* derived from protein carbohydrate and fat The meals that are detailed provide for *75 gm of protein* (300 calories) *200 gm of carbohydrate* (800 calories) and *40 gm of fat* (360 calories) The foods yield adequate amounts of the *minerals* and *vitamins* but there is no harm in supplementing the diabetic dietary by a *multivitamin preparation* or a *yeast concentrate* to assure especially high values for the B complex (p 62?)

Modifications of the basic diet are dependent upon individual requirements Patients in the low income group may be compelled to *reduce the protein quantity* to 50 gm which is still adequate Maintenance of weight may require an *increased caloric intake* which is best provided by an initial *increase of the carbohydrate to 300 gm Later the fat content is augmented* provided that the ratio of grams of carbohydrate to grams of fat never exceeds 2 to 1 The use of a *carbohydrate fat ratio* of 6 to 1 is recommended for patients who are obese the juvenile diabetics those with cholecystitis and cholelithiasis with complicating arteriosclerotic vascular disease and those with recurrent acidosis

Special Foods—The use of special diabetic foods is discouraged There is no reason why the diabetic cannot be fed with the same products as the rest of the family

Sweetening Agents—The use of sweetening agents to taste is permis

Ideal Control—Unfortunately those who specialize in diabetes have made production numbers of the problems of therapy It is their contention that it takes three months to teach the patient to eat quantitatively During these three months there are required the coordinated efforts of physician, nurse dietitian technicians and members of the family The suggested armamentarium includes (*1*) Facilities for performing qualitative tests for the presence in the urine of dextrose and acetone or diacetic acid, (*2*) a reliable method for the quantitative determination of urinary dextrose (*3*) facilities for measuring carbon dioxide combining power and the concentration of dextrose in the blood (*4*) methods for determining the lipoids of the blood, (*5*) examination for total nitrogen and special fractions of nitrogen of the urine (*6*) examination for the non protein nitrogen of the blood for carotene and the various electrolytes (*7*) insulin of unmodified and protamine zinc varieties (*8*) hypodermic syringes and needles, (*9*) one flask of 500 cc of sterile saline (*10*) ampoules of sterile 50 per cent dextrose (*11*) ampoules of epinephrine (1 1000), (*12*) Benedict solution test tubes and alcohol lamps, (*13*) solution of ferric chloride or crystals of sodium nitroprusside and a solution of ammonia (*14*) a stomach tube, (*15*) a primer for the patient with directions and charts for preparing diet prescriptions menus and recipes (*16*) a nomogram for normal metabolism age sex height and weight in order to calculate the diet, (*17*) scales for weighing food, (*18*) measuring cylinders for fluids (*19*) weight scales for the patient

The practitioner of experience realizes the impossibility of meeting these ideal requirements He knows that diabetes is controllable by cruder methods Few patients can afford to weigh and measure their food intakes and it is a rare kitchen that can serve diabetic trays Laboratory control must be reduced to those tests that can be performed by the patient or the housewife Insulin injections must be regulated so that they do not interfere with the pursuit of the normal activities of the normal life The diet must conform to the average American intake of food and since the disturbance is controllable but not curable the medical directions cannot be too rigid or too exacting

Practical Therapy—The suggestions for therapy which immediately follow represent an attempt to compromise between the ideal and what is practicable Except for the initial diagnostic investigation the laboratory controls are within the capacities of the office laboratory and the patient of average intelligence A *basic diet* is outlined in conformance with the eating habits of the average American citizen The necessary foods are present in satisfactory quantities and a proper balance has been established Each patient is given the opportunity of dietary control without substitution therapy If this cannot be accomplished the patient is taught to inject *insulin* and an attempt is made to control the disease by the *single daily injection* of the protamine variety

In conformity with the teachings of Tolstoi a *glycosuria* is maintained in protamine-treated patients Since this method is not universally accepted particularly by those who strive for a sugar free urine its basis theories and practices are only briefly summarized

1 The satisfactory treatment of the diabetic who requires protamine insulin depends upon the quantity of glucose utilized, provided that an optimal weight can be maintained and diabetic symptoms and urinary ketones are eliminated

2 Neither the degree of glycosuria nor the value for the blood sugar furnishes adequate criteria for the regulation of diabetes
3 The patient who oxidizes and stores the quantity of carbohydrate essential for his particular needs approaches the normal state whether or not he has sugar in his urine
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Modifications of the basic diet are dependent upon individual require ments Patients in the low income group may be compelled to *reduce the protein quantity* to 50 gm which is still adequate Maintenance of weight may require an *increased caloric intake* which is best provided by an initial increase of the carbohydrate to 300 gm Later the fat content is augmented provided that the ratio of grams of carbohydrate to grams of fat never exceeds 2 to 1 The use of a *carbohydrate fat ratio* of 6 to 1 is recom mended for patients who are obese the juvenile diabetics those with cho lecystitis and cholelithiasis with complicating arteriosclerotic vascular dis ease and those with recurrent acidosis

Special Foods—The use of special diabetic foods is discouraged There is no reason why the diabetic cannot be fed with the same products as the rest of the family

Sweetening Agents—The use of sweetening agents to taste is permis

sible *Saccharin* (benzo sulfinide) in ¼ to 1 grain tablets augments the palatability of many foods and beverages

Condiments—The diabetic is encouraged to use salt pepper mustards and tomato garnishings These relieve the monotony of the diet and add considerable zest to foodstuffs

Beverages—Most of the nonalcoholic beverages contain considerable amounts of sugar and they are permissible within limitations Diabetics

TABLE 81—LABORATORY CONTROLS FOR THE MANAGEMENT OF DIABETES

Tests Done by Physician

Urine

Routine

Quantitative Sugar (p 3675)
Done at first visit thereafter only a rough estimation is necessary

Acetone and Diacetic Acid (p 3680)
The acetone test suffices for most purposes The diacetic acid reaction need be done only in rare instances

Fermentation (p 3675)
Done at first visit to identify sugar as dextrose If there is a copper reduction without positive fermentation a specimen should be sent to clinical pathologist for spectroscopic examination

Spectroscopy
In doubtful cases the sugar can be identified by the use of the spectroscope

Blood

Fasting Sugar (p 3714)
Required at the diagnostic examination Thereafter the degree of hyperglycemia is of little importance If more than 200 or more mg per cent, there is little doubt about the diagnosis of diabetes mellitus

Sugar Tolerance (p 3716)
Mandatory if the fasting blood sugar is below the 200 level A normal tolerance curve suggests a renal diabetes if there is persistent glycosuria

Tests Done by Patient

Urine

Sugar
By Galatest method which requires only that a drop of urine be placed on a small quantity of the test powder

Acetone
Same as above

Weight

The body weight is of *greatest significance* Overweight patients are encouraged to reduce their caloric intake to the point where they maintain themselves in a state of slight undernutrition Lean diabetics are not encouraged to gain weight Children are to maintain a weight gain in keeping with normal standards (p 2727) Obese diabetics who do not lose weight on low calory diets may need supplementary administration of thyroid extract if the basal metabolic rate is low

who require rigid control may purchase soda pop sweetened with saccharin

Alcohol—The diabetic who is accustomed to partake of alcoholic beverages is not deprived of his small vice provided that his liquor is taken in moderation Cocktails and liqueurs however possess considerable quantities of sugar and the best drink for the diabetic is therefore a whiskey

with water or soda Not more than two normal sized drinks are permis sible within a twenty four hour period

Tobacco—Unless the diabetic has evidences of peripheral vascular dis ease he may continue the use of tobacco in any form

Chewing Gum—Chewing gum often appeases the appetite of the dia betic and provides him with something to do when others are taking sweets

Exercise—The diabetic is urged to keep in good muscular tone flabbi ness in the diabetic predisposes to infection and susceptibility more than in the nondiabetic

Insulin—Sooner or later the majority of diabetics are required to give themselves injections of insulin To this end they are furnished with spe cial *insulin syringes* and *needles* a *syringe case vials of protamine zinc and soluble insulin* and ampoules of *epinephrine* (1 1000)

Special *insulin syringes* are usually of 1 cc capacity In addition to the centimeter scale many are also graduated in terms of insulin unitage The latter is apt to be confusing since the concentrations of insulin vary according to dilution and serious errors may be made Hence the practi tioner should be sure that his patients are furnished the insulin syringe with the simpler calibrations

Diabetics who need only a single daily injection may keep the insulin syringe and its needles in a covered vessel containing alcohol Those who travel or require several daily injections are provided with a *syringe carrying case* preferably one in which the implements can be kept sterile so that boiling is unnecessary

Protamine insulin is marketed in vials with white labels and red letter ing *The U 40 strength* contains 40 units to the cubic centimeter and the *U 80* contains 80 units to the cubic centimeter

Soluble insulin is marketed according to unitage in yellow red and green labeled vials *The yellow contains 20 units the red 40 units and the green 80 units to the cubic centimeter* Globin insulin is available in vials containing 80 units per cubic centimeter

The insulin equipment is completed by ampoules of epinephrine hydro chloride (1 1000) for immediate injection in the event of an episode of hypoglycemia

The Technic of Insulin Injection—Patients are taught the handling of insulin syringes so that they become adept in the self injection of the hormone They are instructed in the technic of sterilizing assembling and loading the syringes Injections are best made in different sites on the anterior and median aspect of the mid thighs after sterilization of the skin area by vigorous rubbing with alcohol Following injection the equip ment is returned to the sterile container to be made ready for subsequent injections

The most important technical considerations in the insulin injection is that the needle requires introduction at right angles to the skin We prefer to spread rather than pinch the skin and render it taut before in troducing the needle

The Treatment of Uncomplicated Diabetes on the Basic Diet—The diabetic who has a glycosuria but no ketosis is placed on the basic diet for a mini mal period of three days The required observations are relative to the

sible *Saccharin* (benzo sulfinide), in 1/4 to 1 grain tablets augments the palatability of many foods and beverages

Condiments—The diabetic is encouraged to use salt pepper mustard, and tomato garnishings These relieve the monotony of the diet and add considerable zest to foodstuffs

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TABLE 84—LABORATORY CONTROLS FOR THE MANAGEMENT OF DIABETES

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who require rigid control may purchase soda pop sweetened with saccharin

Alcohol—The diabetic who is accustomed to partake of alcoholic beverages is not deprived of his small vice provided that his liquor is taken in moderation Cocktails and liqueurs however possess considerable quantities of sugar and the best drink for the diabetic is therefore a whiskey

tient ambulatory However marked acetonuria and the presence of acidotic manifestations require hospitalization and intensive treatment

Diabetes Complicated by Acidosis With Few or No Symptoms and a Slight Acetone Reaction —1 To the basic diet add 3 to 6 gm of *table salt* given in tablet or capsule form several cups of *salty broth* and at least 2 to 3 additional quarts of water or an *alkaline beverage*

2 If the urine test for sugar is yellow red (2+ per cent) give an additional immediate injection of *soluble insulin U 25* and be prepared to administer a large glass of *orange juice* if manifestations of hypoglycemia become manifest

3 If the urine test for sugar is green yellow (less than 1 per cent) give an additional immediate injection of *soluble insulin U 15*

4 If the urine test for sugar is negative despite acetonuria give the *orange juice* without insulin

5 When the acetonuria has been controlled resume the basic diet and the standard protamine insulin dose but seek an explanation of the acidotic complication The possibilities include errors in diet or insulin dosage fatigue emotional or physical strain the presence of a systemic infection such as an upper respiratory infection or a tuberculosis a local infection such as a pyoderm or a dermatophytosis pregnancy or the onset of a hyperthyroidism

Diabetes Complicated by Acidosis With a Heavy Acetone Reaction and Moderate Symptoms but Without Coma —1-5 same as for diabetes complicated by acidosis with few or no symptoms and a slight acetone reaction (p 3680)

6 Immediate hospitalization

7 Start an intravenous infusion of 5 per cent glucose in saline with 1 unit of soluble insulin for each gram of the infused dextrose

Diabetic Coma —1-7 same as for diabetes complicated by acidosis with a heavy acetone reaction and moderate symptoms but without coma (see above)

8 As soon as possible substitute *Hartmann s solution* for the glucose in saline The Hartmann s solution is commercially available in ampoules which must be diluted with 25 volumes of sterile distilled water saline or saline in glucose before intravenous injection

9 If the coma is profound inject 20 to 50 cc of 50 per cent dextrose using a large syringe whose needle is plunged through the rubber tubing of the infusion set

10 Inject subcutaneously *protamine insulin U 50 to 100* and at another site *soluble insulin U 20* always being prepared at any given time to repeat the intravenous injection of the 50 per cent dextrose if a hypoglycemia develops

11 Maintain body warmth with *warm blankets* but avoid electric pads and hot water bottles which may produce burns

12 Be watchful for *acute dilatation of the stomach* and *urinary retention* On suspicion perform a *gastric lavage* and a *bladder catheterization*

weight the subjective symptoms and the presence of glycosuria or ketonuria

1 Those diabetics on the basic diet who *maintain their weight lose their diabetic symptoms* and reveal *negative tests of the urine for sugar and acetone* are regarded as satisfactorily controlled at least temporarily They are cautioned to adhere to the diet and do weekly urine analyses They report to the physician upon the reappearance of glycosuria or suggestive symptomatology

2 Diabetics on the basic diet who reveal *progressive weight loss continuation of symptoms* persistence of *glycosuria* or the development of *acetonuria* require substitution therapy with insulin To this end they are provided with the necessary equipment (p 1255) and a vial of protamine insulin U-40 On each of three successive mornings before breakfast 0.5 cc of the protamine insulin yielding 20 units of the product is injected and the basic diet is supplemented by a feeding of milk and several crackers at bedtime The patient is cautioned concerning hypoglycemic reactions and carries tablets of dextrose or an orange for immediate ingestion upon the appearance of even suspicious symptoms

3 The diabetic on the basic diet with his dose of protamine insulin of U 20 who *maintains his weight* satisfactorily *loses his diabetic symptoms* and whose *urine is free from acetone and glucose* during the three day period is instructed to decrease the insulin dosage for another three day period to U 15 then U 10 and then U 5 until a glycosuria is again observed The resumption of glycosuria is assurance of protection against hypoglycemic reactions The innocuousness of its persistence has been detailed at length elsewhere (p 1252)

4 The diabetic on the basic diet with protamine insulin U 20 who remains *symptom free with satisfactory weight* and who has *glycosuria but no acetonuria* is regarded as being in a state of satisfactory control

5 The diabetic on the basic diet with protamine insulin U 20 whose *weight is not satisfactory* or who has *persistent symptoms* or *acetonuria* is unsatisfactorily controlled and his insulin dosage is increased by U 5 every third day until the conditions of No 4 (above) are accomplished If more than 30 units are required and there is a fasting glycosuria soluble insulin is used additionally in the proportion of 1 unit of soluble to 2 units of protamine

Those patients who are satisfactorily controlled as in paragraphs 1 3 4 and 5 receive instructions and admonitions regarding the possible development of hypoglycemic episodes or acidosis They are warned that vigilance must be maintained by daily and later weekly urine analyses and the monthly submission of a specimen to the physician They are cautioned against failing to report the onset of any discomfort infection or injury no matter how trivial

The Treatment of Diabetes Complicated by Acidosis—The practitioner is justified in treating asymptomatic acidosis of a mild degree with the pa

is a good likelihood that a nonreacting preparation will be found If none can be injected without allergic responses the patient must be desensitized by the intracutaneous method as elsewhere described (p 563)

Atrophy of the subcutaneous fat tissue at the site of insulin injections has been described but is a rare complication

Insulin Resistance—A high degree of tolerance to the hypoglycemic effects of insulin occasionally arises Acidosis hepatic disease infection and certain endocrine disorders decrease sensitivity to insulin and demand a marked increase in insulin requirements Interference or destruction of the hormone is attested by the injection of 400 to 2000 units in a single day during an insulin resistant phase The experiment of Houssay in the effects of removal of the anterior pituitary gland on insulin sensitivity suggests that the disturbance may be in the nature of a hormonal antagonism

The Preparation of the Diabetic for Surgery—The diabetic who is to have an operative procedure of choice is admitted to the hospital several days before the projected operation He is given a *richer carbohydrate diet* and an abundance of *salt* and *fluids* These requirements are met by administering 200 cc of orange juice with 10 units of soluble insulin between each of the principal meals with 200 cc of water and 1 gm of table salt about one half hour before the fruit juice and again at bedtime

Supplementary *basal anesthesia* is clearly indicated particularly if it is possible to do the procedure under *local or spinal anesthesia* (p 3012) *Inhalation anesthesia* has the disadvantage that the patient cannot resume normal feedings upon his return from the operating room

If an inhalation anesthesia is used an intravenous drip is established in the operating room After the first 500 cc of 5 per cent dextrose in saline solution have run in a subcutaneous injection is made of soluble insulin U 25 On the return of the patient to his room an indwelling catheter is placed in the bladder and the urine specimens are tested for acetone and sugar at hourly intervals From this point on the management is the same as for a *diabetic acidosis* (p 1257) A yellow reduction with acetonuria calls for the immediate injection of soluble insulin U 20 to 25 a green reduction requires only 10 units If the patient is sugar free orange juice is administered to assure a sufficient amount of carbohydrate for combustion The presence of glycosuria of itself need not cause concern unless it exceeds 2 to 3 per cent Under those circumstances 1 unit of soluble insulin is administered to each 1 to 2 gm of excreted sugar As soon as possible the basic diet is resumed with the preoperative dose of protamine insulin

Diabetes and Infection—The diabetic is said to be very susceptible to infections *Boils carbuncles chronic epidermophytosis acute pneumonia acute pyelonephritis* and *pulmonary tuberculosis* are stated to be more common in diabetics than in the general population These views are opposed by statistics which reveal no significant change

Infection has a profound effect on the severity of diabetes It decreases the effectiveness of insulin and often leads rapidly to coma Any sudden change for the worse in the status of a diabetic should lead to a careful search for an infective focus Urinary tract infections and tuberculosis are often obscure and escape recognition unless sought

13 Avoid complicating the clinical picture by the injection of powerful drugs such as morphine codeine digitalis caffeine strychnine coramine

14 Be alert to the possibility of *water intoxication* or the *bulk reaction* (p 705) due to the intravenous infusion The appearance of these manifestations requires interruption of the intravenous medication

Diabetes Control Without Glycosuria —Those who aim to keep the urine sugar free under all conditions run the hazard of the production of *hypoglycemic shock* Additionally the patient is under the constant strain of contriving to have clear specimens and suffers varying degrees of anguish when the tests show a reduction If as Tolstoi states the important principle of the regulation of carbohydrate metabolism resides in the amount of sugar burned *and not what spills over into the urine* then this refinement is not worth the effort that it requires An exception to this statement exists when the diabetic has associated urinary or gynecological infection Under these circumstances bactericides may be more useful in *the absence of urinary sugar*

Freedom from glycosuria may be accomplished by altering the diet or the dose the type or the time relationship of the insulin injection In the event of a glycosuria the amount of food may be cut down, the dose of *insulin may be increased the injection may be made earlier or later* with reference to meals a combination of protamine and soluble insulin or an additional dose of protamine insulin may be tried

It is our opinion that the basic diet should be maintained and the *changes made with the insulin If the protamine insulin is given early* in the morning and significant glycosuria occurs after breakfast it is necessary to give a dose of soluble insulin at the same time If the significant glycosuria occurs in the evening or early in the morning it is the pro*tamine dose that must be increased*

The determination of these diurnal variations requires the separate examination of several voidings and very few patients have the time or zeal to go to that amount of trouble If a second dose of insulin has to be *given many patients object to the double injection since it* is generally agreed that different sites are to be employed for the protamine and the soluble preparations

Treatment of Insulin Shock —Hypoglycemic reactions are bound to occur in the *forms of diabetic management that aim at eliminating glycosuria* The patient is made aware of the early symptoms which include nervousness restlessness sweating faintness and hunger The instant these make their appearance sugar candy orange juice or some other readily available *form of sugar* is swallowed The patient is prepared for this emergency by having preparations in pocket or handbag If there is time a subcutaneous injection of 0 5 cc of epinephrine 1 1000 is administered

Should the patient s attempts prove unsuccessful the physician injects *dextrose* in 50 per cent solution intravenously and gives the epinephrine subcutaneously

Insulin Hypersensitivity and Atrophy —Anaphylactic reaction to insulin can occur as with the parenteral administration of any other foreign protein Under these circumstances, another brand of insulin is tried and there

is a good likelihood that a nonreacting preparation will be found If none can be injected without allergic responses the patient must be desensitized by the intracutaneous method as elsewhere described (p 563)

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With the mildest systemic or local infection the diabetic is confined to bed The basic diet and the insulin dosages are continued but soluble insulin is added when indicated as in the management of the surgical diabetic or in acidosis

The development of *tuberculosis in a diabetic* makes dietary control more difficult and calls for additional dosages of insulin If the tuberculosis is sufficiently severe to require bed rest the patient has plenty of time and leisure to make urine tests and accomplish freedom from glycosuria The same principles apply when *the tubercular patient develops diabetes* during the course of his infection Metabolic control should be easily possible and the course of the bacillary process need not necessarily suffer

Diabetes and Pregnancy—Before the use of insulin the fertility of the diabetic was low and pregnancy was a rarity There was a high incidence of *abortions* and *stillbirths* Since the use of insulin pregnancy is frequent in diabetic patients Although the maternal mortality has been reduced to a level comparable to that in nondiabetics the *fetal death rate* is still high The *fetus* of the diabetic mother is usually large and may weigh 12 to 18 pounds The infant is often *stillborn* and *macerated* at birth The large size of the fetus makes delivery difficult and increases the frequency of *birth injuries* and *cesarean sections* After birth the infant is prone to *hypoglycemic seizures* possibly as a result of hypertrophy of its islet tissue *Congenital diabetes* in the offspring of diabetic parents has been observed but is rare

The pregnant diabetic may experience a sudden increase in the severity of the disease and may rapidly lapse into diabetic coma On the other hand pregnancy has been known to ameliorate the disease The phenomena observed during pregnancy in diabetics have been ascribed to the endocrine imbalance present in these patients There is evidence that an abnormal rise in chorionic gonadotropin precedes premature delivery stillbirth neonatal death sudden toxemia with hydramnios the delivery of a macerated stillborn child and the premature delivery of a mature appearing atelectatic infant which dies within a few hours after birth These accidents may be prevented by the continuous administration of *estrogen* and *progesterone* during the last two months of the gravidity

Impregnation of the diabetic may result in increased or decreased insulin resistance If the metabolic condition becomes ameliorated it may be necessary to reduce the dose of protamine insulin in order to prevent a hypoglycemic reaction If the pregnancy increases the glycosuria the dose of protamine insulin must be augmented to prevent complications in the mother and to reduce the possibility of a compensatory hyperplasia of the fetal insular tissue

The onset of diabetes during pregnancy is not uncommon but great care must be taken not to mistake the lactosuria for diabetes In the former instance the blood sugar tests are normal and the urinary reaction reveals that the reducing substance is not dextrose The principles of therapy elsewhere outlined (p 1251) need not be altered except that it is important to maintain a sense of well being on the part of the patient absence of acidosis and normal weight gain

The Neuropathies—The diabetic neuropathies are likely manifestations

of vitamin deficiency In addition to giving large amounts of the crude vitamin B complex by mouth in a yeast concentrate *thiamine chloride* is injected intravenously in amounts of 100 mg. daily Additionally nicotinic acid is provided

Diabetes and Obesity—The obese diabetic is given a diet with exceedingly low fat perhaps in the ratio of 6 gm of carbohydrate to 1 gm of fat this reduces the caloric intake and assures weight reduction An estimation of the basal metabolic rate is done so that *thyroid extract* may be ordered as indicated

Diabetes and Disease of the Gallbladder—The diabetic with gallbladder disease is treated in the manner of the obese patient Removal of the diseased viscus may have both immediate and remote beneficial effects

Diabetes and Peripheral Vascular Disease—The control of diabetes requires that extraordinary efforts be made to prevent peripheral vascular disturbances To that end the patient is given instructions as to foot hygiene The general principles are undernoted

1 Only well fitting shoes are worn Barefoot walking is forbidden
2 Tight shoes which cause pressure points are discarded
3 Loose shoes which cause friction are discarded Metal arch supports are avoided
4 Socks with darns and holes are avoided The best sock is one made of lisle In cold weather a woolen sock may be drawn over the lisle sock
5 Circular garters are avoided Adhesive plaster must not be applied to the skin
6 The shoes are laced snugly but neither too tight nor too loose The lining of the shoe is examined so as to avoid friction due to defects or folds
7 The feet are washed frequently in warm but not hot water and scrubbed with soap and water Particular attention is given to the region of the nails and the interdigital areas After washing these same areas are thoroughly dried by patting but not rubbing and powdered At bedtime it is well to anoint the feet with oil The toenails are cut square The tendency to ingrowing or incurving is prevented by gently inserting a cotton wick until the nails grow out
8 Many large communities have expert chiropodists who do excellent work in foot hygiene and who can be relied upon to refer any but the simpler afflictions to the physician All too many however take it upon themselves to attempt the treatment of dermatophytosis and other disturbances whose care is beyond their province
9 Those who suffer from cold feet are encouraged to take contrast baths (p 3790) They should sleep with bed socks or with their feet wrapped in flannel Electric pads or hot water bottles are avoided Rubbers are worn in inclement weather

Diabetes and Hyperthyroidism—The association of diabetes and hyperthyroidism is most unfortunate since the presence of either one of the afflictions adds to the gravity of the other Since the thyroidal disturb

ance is the more easily and satisfactorily remedied the patient is hospitalized and immediately prepared and subjected to adequate surgery (p 1214) With abatement and control of the hyperthyroidism the diabetes may undergo a signal improvement and even complete disappearance

During the course of the operative procedure the management of the diabetic is as previously described (p 1251) The most unusual care and precaution must be exercised however since violent changes may occur in brief periods of time particularly if there is a superimposed thyrotoxic crisis

RENAL DIABETES

Renal diabetes (*benign glycosuria diabetes innocens*) is a benign hereditary and familial metabolic defect Its essential cause is unknown and it is described in the present section merely for convenience and by way of contrast with the condition of diabetes mellitus

Clinical Manifestations—In renal glycosuria it is assumed that the permeability of the kidneys for glucose is increased More likely the defect represents an inadequate reabsorption of glucose in the renal tubules At any rate the condition is characterized by a persistent *glycosuria without hyperglycemia changes in the sugar tolerance curve* or the *symptoms of diabetes mellitus*

See *Differential Diagnosis of Glycosuria* (p 3676)

Renal diabetes is a relatively uncommon disorder that is usually recognized in the course of a routine urine analysis Sugar is present in every specimen of urine whether voided in the fasting state or after a meal Ketosis and impairment of health are not experienced and doses of insulin have little or no effect on the glycosuria

The importance of recognizing renal diabetes rests in the prognosis and treatment The patient can be assured that the condition is benign and has no promise of leading to diabetes mellitus Treatment is not required by diet or injections of insulin The latter in point of fact may be dangerous since they are prone to produce hypoglycemic episodes

CLINICAL DISTURBANCES OF THE INSULAR TISSUE

The clinical disturbances of the pancreas as a whole have been elsewhere described (p 1937) Those lesions which involve the insular tissue predominantly are important only in so far as they produce the functional disturbances of hyperinsulinemia and diabetes mellitus They include adenomas hypertrophy and hyperplasia atrophy and malignancy

Adenomas of the Insular Tissue—The adenomas of the insular tissue are recognized only when an exploration of the pancreatic tissue is made for the relief of the acute episodes of hypoglycemia The condition may be ameliorated by a removal of the neoplasm

Hypertrophy and Hyperplasia of Insular Tissue—See *Hyperinsulinism* (p 1242)

Atrophy of Insular Tissue—Atrophy and peculiar hyaline degeneration of the insular tissue may be associated with diabetes mellitus (p 1246) Nevertheless the metabolic derangement may be present without histological changes and the allegedly specific cytologic phenomena are said to be demonstrable in those who do suffer from the disease These morphological variants in no small part are responsible for the present dis

quieting views on the pathogenesis of the disturbances of carbohydrate metabolism (p 782)

Malignancy —Malignancy of the insular tissue may give rise to rapidly progressive manifestations of hyperinsulinemia or they may be associated with a rapidly progressive diabetes mellitus (p 1246)

Surgical attempts at removal are worth the effort since the prognosis is otherwise hopeless

THE ADRENAL GLANDS

THE ADRENAL MEDULLA

The adrenal medulla constitutes the *inner layer* of the adrenal glands whose structure is more completely described in the consideration of cortical abnormalities (p 1260) The dark brown medulla is soft and pulpy It is phylogenetically an *autonomic ganglion* and as such receives preganglionic fibers from the adrenal plexus and the splanchnics

Histologically the medulla consists of irregular groups of *chromaffin* cells separated by profuse networks of vascular sinusoids The term chromaffin is suggested by the brownish coloration assumed by these cells when treated with the salts of chromic acid They are colored green by ferric chloride (*Dulpian reaction*) These color phenomena are due to the presence of epinephrine the product of the medullary cells

Epinephrine Chemistry Pharmacology and Therapeutics —See p 3877

Physiology —With the discovery of *epinephrine* in 1894 attention was focussed on the adrenal medulla almost to the exclusion of the cortex It was natural to assume that the potent pharmacological effect of epinephrine particularly in vascular tension was significant in clinical mechanisms These inferences led to the interpretation of hypertension as a hyperadrenalemia and conditions of hypotension particularly the Addisonian syndromes were regarded as insufficiencies of the medullary substance Surgeons were stimulated to perform excisions of the adrenal medulla or denervations in the attempt to control hypertension Addison s disease was treated by injections and rectal and oral administrations of epinephrine

Probably no bright and shining medical hypothesis ever suffered so rude an awakening The first suspicion of the tenuous basis of the theories of medullary function followed the demonstration that the adrenal medulla was not essential to life Next the concentration of epinephrine in the blood during rest and under physiological conditions was proved to be no greater than 1 2 000 000 000 to 1 1 000 000 000 dilutions which have no demonstrable effect on the intact normal animal

Emergency Theory—Faced with these indubitable facts Cannon postulated the theory of the *emergency functions* of the adrenal medulla It was his belief that the animal during the necessity for defense or attack poured out epinephrine thus producing an elevation of blood pressure mobilization of carbohydrates increased oxygen capacity of the blood bronchiolar dilatation a shortened coagulation time and the emotional manifestations that accompany situations of stress and strain The Cannon theory suggested to the surgeons that denervation of the adrenals might be expected to ameliorate conditions such as diabetes mellitus hyperthyroidism and hypertension

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may rise to 300 systolic to 180 diastolic The patient appears anxious apprehensive and close inspection reveals erection of the body hairs (pilo motor response) A prolonged episode is poorly tolerated and may lead to profound shock (epinephrine collapse)

Laboratory Findings—During an attack the blood sugar is elevated and there may be glycosuria By perfusion experiments it has been possible to detect a pressor substance probably epinephrine in the blood in increased concentration during an attack Following removal of a pheochromocytoma large amounts of pressor substance have been recovered from the tumor tissue which gives an intense chromaffin reaction

Diagnosis—The diagnosis of pheochromocytoma is suggested by the paroxysmal evidences of hyperepinephrinemia and the finding of a palpable mass in the flank An attack may be induced by massage of the mass change in the patient s position or a dose of insulin In likely cases the diagnosis may be established by roentgen evidence of an adrenal mass and contrast visualization of the kidneys A peri renal air insufflation is of value in visualization of the tumor by x ray

Differential Diagnosis—A pheochromocytoma must be differentiated from other conditions causing paroxysmal hypertension and autonomic nervous discharges These include *autonomic diencephalic epilepsy* usually associated with a tumor of the third ventricle *idiopathic epilepsy* (especially in some patients with petit mal attacks) and in the early phases of accelerated arterial hypertension It is also possible that the syndrome may result from lesions causing acute transient renal ischemia

Treatment—Removal of the offending tumor produces a prompt and dramatic cure The postoperative course is often stormy and attended by the sudden onset of severe shock as soon as the tumor pedicle is clamped To prevent this the patient is given a continuous infusion of normal saline containing sufficient epinephrine to maintain the blood pressure at a normal level

Neuroblastomas—The neuroblastomas of the adrenal medulla are seen in children under the age of four The tumor is often bilateral and the microscopic appearance is that of a *sarcoma*

The clinical manifestations are variable In the *Pepper type* there is a *hepatomegaly* with involvement of the mesenteric lymph nodes and a rapidly fatal course in a few weeks In the *Hutchinson variety* there are metastases in the skull and orbit with resultant rapidly increasing *proptosis* and hemorrhagic phenomena in the eye This tumor is also highly malignant and there is no available therapeutic approach

Ganglioneuromas—The ganglioneuroma is a benign medullary tumor that occurs in children and adults It is found in the brain and abdominal sympathetics as well as in the adrenal gland

The Adrenal Cortex

The adrenal cortex is vital to the normal economy and life cannot be sustained after ablation of the cortical tissue *Adrenal cortical insufficiency* gives rise to the Addisonian syndrome and *hyperactivity* produces virilism and manifestations of hypertension Despite its protected position the cortical tissue is the site of a variety of pathologic processes which include *hyperplasia benign and malignant neoplasms infections* such as

While there is popular acceptance of the Cannon emergency theory many who have worked in this field including the senior author have never been satisfied that the concentrations of blood epinephrine can be increased to effective levels Certainly the hypothesis is not sufficiently proven to warrant surgical interference with the adrenal medulla in any of the clinical disturbances for which the procedure has been recommended and attempted In support of this critical attitude is the failure of surgery to demonstrate any consistent and significant amelioration of any of the symptoms for which the operation has been performed

A viewpoint consistent with present knowledge is one that would attest to the *pharmacological potency* of epinephrine and admit the possibility that the substance has *functional and hormonal potentialities* Beyond this lies the twilight zone of endocrinology

Hyperadrenalemia —The problem of *functional or emergency hyperadrenalemia* under physiological conditions has been discussed in the previous paragraphs The possibility that *pheochromocytomas* may be instrumental in the production of an *intermittent paroxysmal hypertension* is discussed in the later section on neoplasms of the adrenal medulla (p 1264)

Hypoadrenalemia —Until the significance of the adrenal cortical hormone became obvious it was the general belief that hypo adrenalemia was responsible for *Addison's disease* and perhaps also for certain types of *neurasthenia* characterized by *hypotension* There is now general concurrence regarding the insignificance of the role of the adrenal medulla and the great importance of adrenal cortical hormone (p 1267) To the best of present knowledge there are no clinical implications relative to deficiency or even absence of adrenal medullary secretion

NEOPLASMS OF THE ADRENAL MEDULLA

Tumors of the adrenal medulla are rarely encountered The reported varieties include pheochromocytomas neuroblastomas and ganglioneuromas

Pheochromocytomas (Chromaffinomas) —The pheochromocytoma of the adrenal is a benign encapsulated tumor that is commonly associated with the production of paroxysmal hypertension This interesting clinical syndrome is due to the liberation of an epinephrine like substance

Pathology —Pheochromocytomas are benign tumors composed of chromaffin tissue They are usually unilateral well encapsulated and cystic The tumor may completely replace the ipsilateral adrenal but at times is found in the vicinity of a normal adrenal In some cases it is a chance finding in routine autopsies on elderly patients

Clinical Manifestations —The classical clinical features of the syndrome produced by an adrenal pheochromocytoma are evidences of repeated attacks of *intense paroxysmal vasoconstriction* These include sudden pallor intense headache nausea vomiting apprehension loss of consciousness and a marked rise in systolic and diastolic blood pressures The episodes may occur once or twice daily and may last for a few minutes or as long as several hours The attacks are precipitated by sudden changes in position (bending), exercise hunger emotion and in the absence of definite cause During an attack there are well marked evidences of hyperepinephrinemia the skin is cold and pale the pupils dilated the palpebral fissures widened and the eyeballs prominent the pulse is rapid the blood pressure

ADRENAL CORTICAL HORMONES

Preparations —The first available adrenal cortical preparations were crude extracts obtained by extracting the glands with an organic solvent miscible with water They were capable of prolonging life in adrenalectomized animals They caused a retention of sodium chloride and an increased renal excretion of potassium in adrenalectomized and in normal animals Adrenal Cortex Extract (Upjohn) has been accepted in N N R

Recent chemical investigations have demonstrated that the activity of the crude adrenal cortical extracts is due to a mixture of active principles About twenty steroid principles have been isolated from the adrenal cortex These include several *androgens* (adrenosterone) *progesterone* and at least four compounds which can prolong the life of the adrenalectomized animal (desoxycorticosterone corticosterone dihydrocorticosterone and 17 hydroxy 11 dehydrocorticosterone) No one of these compounds can produce all the effects of the whole gland It is not known whether the cortex prepares a number of separate hormones each with a specific function or whether these steroids are derivatives of a single parent hormone and the result of its degradation during extraction and isolation

TABLE 83 —THE ADRENAL CORTICAL EXTRACTS

Product	NaCl Retaining Effect	Carbohydrate Effect
Adrenal Cortical Extract N N R	Present	Present
Corticosterone	Moderate	Moderate
11 Desoxycorticosteron	Strong	Absent
17 Hydroxycorticosterone	Absent	Strong

Desoxycorticosterone Its Chemical and Pharmacological Properties — Adrenal tissue yields small quantities of this steroid The chief source is stigmasterol a sterol found in soy beans from which it is synthetized by oxidation Desoxycorticosterone is very similar in chemical structure to progesterone from which it differs by the presence of an additional atom of oxygen Esterification with fatty acids (acetic propionic) increases the potency and prolongs the action The acetic acid ester is commonly used It is ineffective by mouth and is usually administered in oil (peanut sesame) by intramuscular injection It is insoluble in water soluble in ether alcohol and propylene glycol

Desoxycorticosterone in propylene glycol may be administered sublingually Pellets implanted subcutaneously afford adequate replacement therapy in adrenal insufficiency Desoxycorticosterone has the greatest electrolyte regulating and life maintaining potency of the crystalline compounds derived from the cortex A daily dose of 1.5 mg is sufficient to maintain an adrenalectomized dog in good condition on a salt poor diet

In animals with adrenal insufficiency and in patients with Addison's disease it causes a striking retention of sodium chloride retention of water an increase in the renal excretion of potassium an increase in plasma

tuberculosis and syphilis *hemorrhagic necrosis* and manifestations of metabolic disorders including *amyloidosis* and *hemochromatosis*

Anatomy—The adrenal glands are small triangular structures lying in close proximity to the upper poles of the kidneys Occasionally both glands are fused or there may be a complete agenesis of one gland In addition to the two main structures accessory adrenal tissue predominantly cortical may be found in the peritoneal cavity beneath the right pole of the kidney in the right lobe of the liver within the solar and renal plexuses or on the posterior abdominal wall Each gland consists of a firm reddish brown *cortex* and the *medulla*

The glands are richly supplied with blood from the adrenal renal and inferior phrenic arteries The right adrenal vein empties into the inferior vena cava and the left into the renal vein The glands are innervated from the adrenal plexus via the splanchnics

The histological structure of the cortex is complex Three distinct cellular zones are recognized The *glomerulosa* lying just beneath the capsule consists of rounded groups of cells the *fasciculata* continuous with the zona glomerulosa is the largest part of the cortex and its cells arranged in radial columns are rich in lipoid the *reticularis* is a loose irregular cellular network of well-defined rounded cells with a coarsely granular vacuolated cytoplasm The cortical cells are the source of the *adrenal cortical hormone* Secretory activity appears to be under the control of *anterior pituitary hormone*

Physiology—The adrenal cortex is essential to life Its secretion is concerned with the distribution and excretion of body water and electrolytes carbohydrate metabolism the work efficiency of skeletal muscle the maintenance of a normal level of blood pressure and renal function In addition it affects the function of the gonads the normal pigmentation of the skin and the ability to resist environmental stresses such as cold and pain

Cortical deficiency results in a loss of sodium and water in the urine a depression of the blood sodium level and hemoconcentration The decrease in extracellular fluid is associated with an increase in the intracellular fluid As sodium is lost in the urine the renal excretion of potassium decreases and the concentration of serum potassium rises There is an increased sugar tolerance sensitivity to insulin a flat glucose tolerance curve hypoglycemia and a depletion of liver glycogen

The disturbances in water electrolyte and carbohydrate functions that result from cortical deficiency lead to *adynamia* indicated by a decrease in the work efficiency of skeletal muscle and to focal and diffuse signs of dysfunction of the central nervous system

Low blood pressure faulty postural adaptation and vasomotor collapse are seen in cortical deficiency These abnormalities are not due entirely to the salt water and carbohydrate defects but may result from a local disturbance of the function of the peripheral vessels or from a central disturbance of the vasomotor apparatus The ability to withstand changes in environmental temperature painful stimuli and allergic phenomena is impaired in adrenal insufficiency as is the proper functioning of the gonads and the pigmentary cells of the skin

The administration of potent cortical extracts (see p 1267) to adrenalectomized animals produces sodium retention with an elevation of serum sodium potassium diuresis with a fall in the serum potassium concentration The potassium content of muscle falls while that of sodium increases The blood volume increases and water passes from the cells to the tissue spaces The normal level of glycogenesis dependent on the conversion of protein into carbohydrate, is restored by the cortical secretion

a decrease in urinary androgen excretion is usually apparent within three weeks

Pathology—The commonest lesion productive of adrenal virilism is a *benign hyperplasia* of the adrenal cortex The disturbance may be unilateral or bilateral causing the gland to increase to three to four times its normal size *Adenomas* are rare and vary in size from a small bean to a large palpable tumor They are encapsulated firm and have a bright yellow color *Carcinomas* are more common and are likewise yellowish growths but of varying consistency The cells of these tumors if virilizing give a positive *Ponceau fuchsin* reaction At the same time the pituitary gland often reveals small basophile adenomas with a hyalinization (*Crooke's change*) The ovaries and uterus are small and infantile There may be a persistent thymus The other endocrines are not remarkable

Clinical Manifestations—The clinical features of the adrenogenital syndrome vary with the age of the patient at the onset and the condition of the reproductive organs The most marked changes occur in infancy and childhood The principal manifestations are hypertrichosis and changes in body contour and in the female genitalia

Hypertrichosis—The appearance of an excessive growth of hair is often the first sign of virilism The hair is similar to that of the male in texture and distribution It usually begins on the face and spreads to the legs and thighs and from the pubic region to the umbilicus Patches appear on the chest and back around the nipples over the shoulders and lumbosacral regions With the full development of hirsuties there is a tendency to baldness and temporal recession as seen in the male

Changes in Body Contour—At or shortly after puberty marked alterations occur in the normal female contour Young girls give the appearance of virile and sturdy masculinity and are usually short thick set broad shouldered and deep chested with narrow hips and marked muscular development If normal puberty has occurred the changes are less marked The skin becomes coarse and dry and bears many acne lesions The pelvic girdle is narrow and has a male configuration the breasts regress or remain small and undeveloped the voice deepens and the larynx enlarges Changes similar to these are caused by the administration of testosterone propionate (p 2401)

Genital Changes—The sex reversal is revealed by enlargement of the clitoris and a decrease in the size of the labia and vagina The clitoral hypertrophy varies from a simple enlargement to a well defined penis like structure with a groove on its ventral surface There may be a definite prepuce The uterus is small and infantile and the cervix is hard and buttonlike The vaginal introitus is difficult to penetrate At laparotomy the ovaries are usually small fibrotic and cystic The gonadal insufficiency results in a primary or secondary *amenorrhea*

Pseudohermaphroditism—The intensity of the masculinization is determined to a great extent by the age of the patient at the onset of the adrenal lesion In the most complete forms there is a *pseudohermaphroditism* (p 2081) due to increased androgenic activity during embryonic life The patient has female generative organs and male secondary sexual characteristics The infant has the appearance of a cryptorchid male with a hypospadiac penis The latter is actually a long clitoris with a urethral orifice at its base There may be no vaginal orifice or a small one opening into the urethral meatus The ovaries and uterus are present but remain undeveloped The patient is usually raised as a male is psychologi

volume and a rise in blood pressure The defect in carbohydrate metabolism characteristic of adrenal insufficiency is not affected

In normal individuals the results are qualitatively the same When given with sufficient sodium chloride moderate as well as excessive doses produce a diabetes insipidus like condition in which the sensitivity to pitressin is reduced Excessive doses lower the serum potassium concentration and lead to "periodic paralysis" Progestational effects (development of a uterine secretory endometrium and mammary growth) are produced in the female Large doses produce adrenal atrophy The effects of overdosage of desoxycorticosterone acetate in Addison s disease are mentioned in a subsequent section (p 1277)

The oxygenation of desoxycorticosterone (in positions 11 and 17) increases its carbohydrate regulating potency, but decreases its electrolyte and life maintaining effects An excess of these steroids leads to hyperglycemia and may be responsible for certain features of the adrenal cortical syndrome (see Testosterone p 2401) The steroids with carbohydrate effects are not available in sufficient quantity for clinical use

Therapeutics—Crude cortical extracts and desoxycorticosterone acetate are the only preparations obtainable for therapeutic purposes The chief indication for the use of these substances is the treatment of Addison s disease Their use has been advocated in postoperative shock burns acute infections asthenia and related adynamic states but there is little convincing evidence that they are effective in these conditions

PHYSIOLOGICAL DISORDERS OF THE ADRENAL CORTEX

Pathological variations in the physiology of the adrenal cortex produce the clearly recognizable manifestations of *hyperfunction* which causes *adrenal virilism (adrenogenital syndrome)* and *adrenal cortical insufficiency* most commonly encountered as *Addison s disease* (p 1271)

Adrenal Virilism (Adrenogenital Syndrome)

Hyperfunction of the adrenal cortex frequently gives rise to a condition of abnormal masculinization in the female (*adrenal virilism* or the *adrenogenital syndrome*) The principal feature is the tendency to sex reversal marked by the appearance of the secondary sexual characteristics of the male and the regression of femaleness In some instances the clinical picture is difficult to distinguish from *Cushing s syndrome* (p 1159)

Etiology—Adrenal virilism is caused by the overproduction of *androgenic hormone* or hormones by the cells of the adrenal cortex The basic lesion is usually a *benign hyperplasia* and less commonly a *cortical adenoma* or *carcinoma* The presence of testicular hormone is indicated by the increased urinary excretion of androgens as tested biologically and colorimetrically The responsible hormonal agent is related to but is not identical with the naturally occurring adrenal cortical factors The syndrome probably results from the persistence or reactivation of androgenic tissue normally present in the fetal adrenal cortex between the tenth and twentieth weeks of embryonic life A tumor or hyperplasia is virilizing only if it arises from this androgenic zone which has a strong affinity for the Ponceau fuchsin stain Following adrenalectomy or removal of the tumors

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cally a male and excretes large amounts of androgenic material in the urine A constant finding in these patients is cortical hyperplasia or a tumor of the adrenal cortex (p 1278)

Macrogenitosomia Praecox—In the prepuberal form there is an apparent transfiguration of the female into a virile male with a complete suppression of feminine functions The child is usually somewhat obese, tomboyish overgrown and has a well advanced bone age In an extreme the condition is termed *macrogenitosomia praecox* (p 1185), and corresponds to the Pellizzi syndrome of pineal tumors (p 1184) At puberty the normal female sex changes fail to occur Instead the body hair and contour are of the male type the breasts fail to develop the voice deepens and the clitoris enlarges The condition is steadily progressive

Postpuberal Virilism—The most common variety of the adrenogenital syndrome occurs after puberty The patient who passed through normal puberty experiences a change in her menstrual cycle which becomes irregular scanty and then stops entirely Simultaneously there is a progressive hypertrichosis of the male type a tendency to gain weight and masculine variations in body form voice and genitalia The appearance of these changes is associated with a period of marked emotional distress in which there is a strong sense of shame and despair As a rule the patient shuns the company of others and heterosexual libido is diminished The condition is stationary or mildly progressive when it is due to a simple adrenal hyperplasia In some prepuberal females the adrenal cortical tumor does not masculinize but causes the onset of precocious puberty with menstruation mammary development and a strong heterosexual urge

In some adult patients with an *adrenal cortical carcinoma* the clinical picture is almost indistinguishable from that of *Cushing s syndrome* (p 1159) In addition to masculinization the findings include moderate hypertension a florid complexion acne acrocyanosis purplish striae atrophicae of the lower abdominal wall and a diabetic type of sugar tolerance Hypertrophy of the clitoris is usually present and may be an important point of differentiation from pituitary basophilism (p 1159) In these patients the hormonal imbalance differs from that of other examples of the adrenogenital syndrome in adult females, since large amounts of estrogenic hormone are found in the urine

Diagnosis—A definite diagnosis of virilism emanating from an adrenal hyperplasia or tumor requires demonstration of the offending lesion by radiography or laparotomy Intravenous pyelography is of value in the preliminary localization of the site of an upper abdominal mass Large tumors produce a downward displacement of the kidneys and distort the calices The use of *perirenal air insufflation* is often of diagnostic value This procedure involves the introduction of 500 to 750 cc of carbon dioxide into the perirenal space just inside Gerota s fascia near the upper renal pole The gas serves as a contrast medium and allows the adrenal tumor to be delineated with great clarity on the radiograph

Urinary hormonal assays (p 1147) for androgens estrogens and 17 ketosteroids are of diagnostic importance An excessive excretion of androgens suggests a simple hyperplasia or carcinoma of the adrenal cortex A marked increase in the urinary excretion of estrogens has been observed in adrenal carcinomas High urinary values for androgens and 17 keto

steroids were noted in patients with Cushing's syndrome associated with adrenal cortical tumors and low values occur in those without tumor

Treatment—In pronounced virilism an *exploratory laparotomy* is indicated for investigation of both cortical areas In simple hyperplasia the removal of the larger gland is recommended As a result of this procedure the condition becomes arrested and a striking return of female characteristics may be anticipated Adenomas and carcinomas are removed if possible In patients with an adrenal carcinoma or adenoma the contralateral adrenal may be small atrophic or absent

The patient with adrenal virilism is a *poor operative risk* and extremely susceptible to surgical shock and postoperative infection In consequence the pre and postoperative periods are managed in the manner of an impending Addisonian crisis *Desoxycorticosterone* and *cortin* are given in large divided doses 10 gm of sodium chloride and 5 gm of sodium citrate are injected by vein on the day before operation and for several days thereafter

The associate editor who does not subscribe to this routine believes that energetic preoperative and postoperative treatments with adrenal cortical preparations sodium salts and water tend to accentuate the already existent hypercortinism and may predispose to fatal accident According to his views it would seem logical to withhold sodium salts and water preoperatively and increase the intake of potassium Adrenal cortical preparations are used only when there is unmistakable evidence of adrenal insufficiency

Adrenal Insufficiency (Addison's Disease)

The clinical syndrome of adrenal cortical insufficiency was described in 1855 by Thomas Addison as a diseased condition of the suprarenal capsule" Despite the rarity of the disease in general practice its study is worthy of careful consideration since it has been the source of important contributions to the understanding of many fundamental processes pertaining to the metabolism of foodstuffs electrolytes and water

Etiology—It is variously estimated that 60 to 90 per cent of the patients with Addison's disease are victims of *tuberculosis* of the adrenal glands Atrophy of unknown or unexplained origin accounts for the remainder many of whom may suffer from a primary disorder of hypophyseal function with secondary changes in the adrenal cortex Occasionally there have been reports of Addison's disease due to *amyloidosis syphilis metastatic neoplasms hemochromatosis acute fulminating infections* accompanied by adrenal hemorrhages as in the *Friderichsen Waterhouse syndrome* of meningococcemia *bilateral adrenal denervation* for essential hypertension or *surgical removal of an adrenal tumor* in the presence of a contralateral atrophy or agenesis of the opposite gland Acute adrenal insufficiency also may accompany *severe burns* the *shock syndrome* and *altitude sickness* in aviators (Armstrong)

A mild adrenal insufficiency has been regarded as an etiologic factor in chronic fatigue neurasthenia the involutional psychoses and essential hypotension At the present time there is no convincing objective evidence of any true relationship and *specific therapeusis* has not been consistently effectual

Pathology—The commonest adrenal lesion in Addison's disease is *bilateral tuberculosis* of the glands The lesion is seldom if ever primary and is usually the result of a hematogenous spread of the infection from the lung Extra adrenal tuberculous involvement usually is limited and subclinical but there may be evidences of active pulmonary skeletal hepatic, splenic or lymphatic invasions

Tuberculosis of the Adrenals—The adrenals are frequently enlarged firm and nodular with a mottled grayish red color The capsule is thickened and adherent to the adjacent structures The glands may be so shriveled that they are difficult to find Sections reveal the replacement of normal tissue by areas of confluent caseous nodules separated and surrounded by thin rims of yellow cortical tissue The medulla usually is completely destroyed since it is apparently less resistant to the tuberculous process than the cortex The disease probably starts in the medulla and spreads toward the periphery of the gland Areas of calcification are common and may be extensive Nests or nodules of cortical cells suggest an attempt at compensatory hyperplasia of the remaining parenchyma Tubercle bacilli can be demonstrated in most instances

To produce clinical Addison's disease there must be more than 90 per cent destruction of both glands Unilateral tuberculosis of the adrenal or partial bilateral tuberculosis of the adrenal gland is often observed at autopsy in the absense of any evidence of adrenal insufficiency The facts argue powerfully against the concepts of "formes frustes"

Primary Atrophy of the Adrenals—Primary atrophy of the adrenal is encountered with increasing frequency The origin of the lesion remains obscure but it has been variously ascribed to post inflammatory damage or a sclerotic process analogous to hepatic cirrhosis The condition is a slow degeneration of the cortex marked by the necrosis and disappearance of the cortical cells and replacement by loose fibrous tissue Attempts at regeneration are seen in small adenoma like islands of epithelium Some instances of atrophy are the late results of vascular injuries to the glands following more severe infections or toxemic states Others represent functional failure of the adrenotropic factor of the anterior pituitary

Lesions Other Than in the Adrenals—The pathologic findings in the organs other than the adrenals are not striking in Addison's disease The heart is small and atrophic, sharing in the general emaciation The coronary vessels appear tortuous and the aorta is hypoplastic The stomach and intestinal mucosa are atrophic and frequently ulcerated Often there is a generalized hyperplasia of the lymphatic tissues with persistence of the thymus as in status thymicolymphaticus Slight changes are observed in the other endocrine glands The *thyroid* frequently is the site of degenerative parenchymal change and marked lymphocytic infiltration The ovaries and testes usually are atrophic There are no remarkable changes in the parathyroids or pancreas but the basophile cells of the anterior pituitary show signs of degeneration and may be decreased in numbers

The patient who succumbs in an acute adrenal crisis shows marked hyperemia of the internal organs submucosal hemorrhages and ulcerations of the hollow viscera These findings suggest the presence of a widespread capillary injury and are related to the peripheral circulatory failure that is present before death The kidneys are frequently congested with evidences of tubular atrophy and cytoplasmic granulation Chronic pyelonephritis and renal tuberculosis are often present.

Clinical Manifestations—The *onset* of adrenal insufficiency was described by Addison in the following words The patient in most of the cases I have seen has been observed gradually to fall off in general health he becomes languid and weak indisposed to either bodily or mental exertion the appetite is impaired or entirely lost slight pain or uneasiness is from time to time referred to the region of the stomach and there is occasional actual vomiting which in one instance was both urgent and distressing It is by no means uncommon for the patient to manifest indications of disturbed cerebral circulation

Asthenia—Physical and psychic asthenia are constant early symptoms Fatigue may become so pronounced that most patients are unable to perform even light work or rise from bed This symptom is the clinical counterpart of the decreased work capacity of muscle demonstrated in adrenalectomized rats

Digestive Disorders—*Anorexia* is usually intense the patient experiencing *nausea* at the sight of food There may be a craving for salty foods and an early aversion to fats Epigastric distress bouts of vomiting and periods of alternating diarrhea and vomitings are frequent These symptoms culminate in a progressive *loss of weight* which may amount to 40 or 50 pounds in the course of a few months Peculiar episodes of *intractable diarrhea* associated with spasm of the abdominal muscles are encountered and often simulate an acute abdominal emergency

Neurological Disorders—Nervous and cerebral symptoms constitute interesting aspects of the symptom complex The patient is *apathetic* and easily irritated At times marked *apprehension* and *restlessness* are associated with anxiety The latter symptoms are usually associated with *hypoglycemia* and may precede the onset of *convulsions* or *coma*

Vertigo and *syncope* may dominate the clinical picture These are particularly marked on changing from the horizontal to the erect posture and are associated with a postural fall in systolic and diastolic blood pressures

Gonadal Symptoms—There is a loss of libido in both sexes In the female *amenorrhea* is usually present while the male is *impotent* Pregnancy rarely occurs Should the female become gravid she may experience an amelioration of her disturbances corresponding to the experimental observation that adrenalectomized animals survive longer while pregnant The favorable effects of gestation on adrenal insufficiency are apparently related to the production by the ovaries and placenta of progesterone and other steroids with cortical activity In children the onset of puberty is sometimes associated with a definite lessening of the severity of the disease and this in all probability is related to increase in gonadal activity

Physical Examination—The patient appears wan listless and chronically ill A striking feature is the *pigmentation of the skin* described by Addison as a dingy or smoky appearance or various tints or shades of deep amber or chestnut brown The intensity of the pigmentation varies in different subjects from a light tan to a dark brown that is almost negroid The patient often interprets the change as a suntan and the symptom may be disregarded for a long time The discoloration has a characteristic distribution being most intense in the areas of *normal cutaneous pigmentation* such as the nipples genitalia *pressure points* on elbows knees knuckles and belt line and the *exposed areas* of the face dorsum of hands neck and chest The palms and soles usually escape except for the creases and folds Pigmented moles and black freckles are often superimposed upon the general background of pigmentation

The general increase in pigment deposition affects the mucous membranes of the mouth conjunctiva vagina and anus About the oral cavity it appears as brown or black spots on the lips tongue gums and buccal mucosa The occurrence of pigment in these areas serves to distinguish Addisonian pigmentation from deposits seen in pregnancy carcinomatosis and in peoples of Negroid extraction Pigmentation of the skin and mucous membranes is present in almost every patient but has been absent in examples of adrenal insufficiency confirmed at autopsy In longstanding disease there may be extensive areas of cutaneous depigmentation (vitiligo leukoderma)

The relation of pigment deposition to adrenal insufficiency remains ob

Pathology—The commonest adrenal lesion in Addison's disease is *bilateral tuberculosis* of the glands. The lesion is seldom if ever primary and is usually the result of a hematogenous spread of the infection from the lung. Extra adrenal tuberculous involvement usually is limited and subclinical but there may be evidences of active pulmonary, skeletal, hepatic, splenic or lymphatic invasions.

Tuberculosis of the Adrenals—The adrenals are frequently enlarged, firm and nodular with a mottled grayish red color. The capsule is thickened and adherent to the adjacent structures. The glands may be so shriveled that they are difficult to find. Sections reveal the replacement of normal tissue by areas of confluent caseous nodules separated and surrounded by thin rims of yellow cortical tissue. The medulla usually is completely destroyed since it is apparently less resistant to the tuberculous process than the cortex. The disease probably starts in the medulla and spreads toward the periphery of the gland. Areas of calcification are common and may be extensive. Nests or nodules of cortical cells suggest an attempt at compensatory hyperplasia of the remaining parenchyma. Tubercle bacilli can be demonstrated in most instances.

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The patient who succumbs in an "acute adrenal crisis" shows marked hyperemia of the internal organs, submucosal hemorrhages and ulcerations of the hollow viscera. These findings suggest the presence of a widespread capillary injury and are related to the peripheral circulatory failure that is present before death. The kidneys are frequently congested with evidences of tubular atrophy and cytoplasmic granulation. Chronic pyelonephritis and renal tuberculosis are often present.

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Asthenia—Physical and psychic asthenia are constant early symptoms. Fatigue may become so pronounced that most patients are unable to perform even light work or rise from bed. This symptom is the clinical counterpart of the decreased work capacity of muscle demonstrated in adrenalectomized rats.

Laboratory Data —A mild degree of hypochromic anemia is usually present The degree of actual anemia is difficult to evaluate because of the attendant hemoconcentration There is a moderate degree of lymphocytosis which may be correlated with the general lymphoid hyperplasia or *status thymicolymphaticus*

Basal Metabolic Rate —The basal metabolic rate may be normal or elevated but more commonly it is low There is a definite intolerance to cold and a tendency to hypothermia

Blood Chemistry —Profound alterations occur in the volume and composition of the blood particularly during an acute crisis There are decreases in the concentrations of sodium chloride and bicarbonate and rises in potassium magnesium and urea levels The *nonprotein nitrogen* figure may be several times the normal The *blood cholesterol* may be elevated The fasting *blood sugar* is low and the oral and intravenous dextrose tolerance curves are flattened The hyperglycemic response to epinephrine is impaired or absent and the sensitivity to insulin hypoglycemia is increased The plasma volume is decreased

The changes in plasma *sodium* and *potassium* levels result from increased excretion of urinary sodium from failure of tubular reabsorption and a decreased excretion of potassium due to inability of the kidney to remove it from the blood The diminished *plasma volume* results from an excessive loss of plasma water and base and the movement of extracellular water into the intracellular compartments As a result of the latter the cells contain more water and sodium and less potassium than the normal See *Differential Diagnosis of Hyponatremia* (p 729) *Differential Diagnosis of Hyperpotassemia* (p 731)

Renal Function —The urine is usually increased in volume during the phase of salt and water diuresis In the terminal phases of adrenal insufficiency there is usually an oliguria with urine of low specific gravity the result of severe anhydremia and impaired renal circulation The ability of Addisonian patients to elaborate a concentrated urine is often moderately impaired There is marked delay in the diuretic response to a large volume of water administered by mouth or by vein and correspondingly adrenalectomized dogs appear to be extremely susceptible to *water intoxication*

Course —Unmodified Addison s disease runs a slowly progressive course with a fatal termination in two to four years Some patients have survived ten years or more from the onset of symptoms and others succumb in a few weeks or months Sudden death is frequent and may follow an acute intercurrent infection a surgical procedure exposure to cold or over exertion

Acute Crises —The course is punctuated by dramatic remissions and exacerbations In the *acute crisis* the patient is in a state of peripheral vascular collapse and presents the classical symptoms and signs of *shock* with marked oligemia lowering of plasma sodium and increase in plasma potassium Crises of this type have been attributed to *acute potassium poisoning* and are precipitated in adrenalectomized animals by the administration of large doses of potassium salts Abdominal symptoms during a crisis are frequent and may suggest an acute surgical emergency (p 1748)

Hypoglycemia —The Addisonian crisis occasionally is marked by a hy

scure Skin biopsy shows an abnormal amount of melanin in the cells of the epidermis The pigment probably is formed locally from a precursor of melanin (dioxyphenylalanine or dopa) and epinephrine Pigmentation also has been ascribed to disorder of the metabolism of vitamin C a normal constituent of the adrenal cortex and there is some evidence that it may be due to the abnormal stimulation of the pigment cells of the skin by an overabundance of a *pituitary melanophore hormone*

Cardiovascular Phenomena—The heart sounds are poor and there is a moderate tachycardia The heart is small and the pulse is weak rapid and



Fig 957—Ink spot or melanin pigmentation of the buccal mucosa in a patient with Addison s disease

easily compressible *Hypotension* is usually present even in patients previously known to be hypertensive the blood pressure may be normal however and hypertension has been observed

In the presence of hypotension the ability to maintain an effective blood pressure in the erect posture is often impaired The tension may drop 30 to 40 mm of mercury on changing from a recumbent to an erect position This postural defect usually attended by postural vertigo and syncope may herald the approach of an Addisonian crisis

See *Differential Diagnosis of Hyponatremia* (p 729)

* Therapeutic Notes Courtesy of Parke Davis & Company

oral administration of sodium chloride in doses of 10 gm daily given as enteric coated pills

Desoxycorticosterone—The treatment of Addison s disease with desoxy corticosterone acetate a synthetic adrenal cortical steroid is beset with difficulties The steroid is not the complete adrenal cortical hormone and has no effect on carbohydrate metabolism Despite its use patients with adrenal insufficiency may continue to complain of weakness and asthenia and may have repeated hypoglycemic episodes with fatal termination Occasional patients in whom the state of water and electrolyte and carbohydrate metabolism is normal during therapy with desoxycorticosterone and sodium chloride may die suddenly with a sharp decrease of blood pressure and a rise in temperature but without the usual chemical changes

In addition to its limitation desoxycorticosterone acetate may produce a number of *deleterious effects* Excessive retention of sodium chloride and water produces extreme increases in the volume of extracellular fluid favoring the development of *edema* A rapid increase in blood volume imposes a sudden strain on the weakened myocardium of the Addisonian patient and favors acute cardiac decompensation *Myocardial insufficiency* is further aggravated by the *elevated blood pressure* that is associated with the use of the hormone Muscle weakness leading to *periodic paralysis* may be encountered if the serum potassium concentration is allowed to fall below 1 6 to 2 mg per cent Potassium chloride terminates these attacks

Desoxycorticosterone acetate is capable of prolonging the life of adrenalectomized animals and of rectifying the disturbances in water and electrolyte metabolism It is customary to start treatment with the daily intramuscular injection of 5 mg of desoxycorticosterone acetate in oil supplemented by 8 to 10 gm of sodium chloride by mouth A daily gain in weight of more than one pound during the first few days or more than ½ pound thereafter indicates excessive retention of sodium chloride and water and necessitates reduction of hormone and salt intake The optimal daily dose of desoxycorticosterone acetate and sodium chloride is one that maintains a normal level for the blood electrolytes and body weight without the development of edema or an excessive rise in blood pressure The hormone must be given daily The diet is rich in carbohydrate and a high intake of potassium is maintained to protect against potassium depletion

Subcutaneous Implants—Addisonian patients are also efficiently and conveniently controlled by the subcutaneous implantation of pellets of desoxycorticosterone acetate The pellets weighing about 0 125 mg are placed beneath the skin in the infrascapular region The maintenance dose of desoxycorticosterone is then determined by the daily injection of the hormone in oil while the salt intake is kept at a constant If symptoms of overdosage result the dietary intake of sodium chloride is reduced In the presence of untoward effects removal is indicated

Aqueous Extracts—Aqueous extracts of adrenal cortical substance are presently available Their desoxycorticosterone potency still remains to be demonstrated but they do have the advantage of rapid action and the patient may self administer the dose as with insulin in diabetes

Treatment of a Crisis—For the relief of acute adrenal insufficiency desoxycorticosterone acetate acts too slowly and large amounts of sodium

poglycemic seizure The episode is preceded by malaise and refusal of food and heralded by the onset of restlessness anxiety and disorientation Later the patient develops convulsions and coma with a marked depression of the blood sugar level

See *Differential Diagnosis of Hypoglycemia* (p 734)

Hyperpyrexia—In a certain number of patients the Addisonian death is characterized by a falling blood pressure a soft pulse and profound asthenia These changes are not related to the state of electrolyte and water metabolism they are apparently unrelated to the level of the blood sugar and fail to respond to adequate therapy with active hormonal substances There are noted a terminal rise in fever a sharp decrease in blood pressure and absence of the usual chemical changes suggesting a profound disturbance of the vasomotor apparatus

Diagnosis —The diagnosis of typical Addison's disease is easy to establish Suggestive or atypical early examples require laboratory confirmation

Salt Deprivation Test—The existence of adrenal insufficiency is confirmed by one of a variety of metabolic studies The salt deprivation test involves placing the patient on a diet containing less than 1 gm of sodium chloride per day for three days and measuring the blood sodium level on the morning of the fourth day A positive test is indicated by a fall in the serum sodium concentration from a normal level of 140 m eq per liter to 135 m eq or less This procedure is not devoid of danger since it may precipitate a fatal Addisonian crisis

Culter Power Wilder Test—For the conduct of the Culter Power Wilder test the patient is given a daily diet containing 0 95 gm of chloride 0 59 gm of sodium and 4 1 gm of potassium Water is given freely during the first day and the patient receives potassium citrate (33 mg per kg of body weight) in the afternoon On the second day the fluid intake is reduced to 40 cc per kg and the dose of potassium citrate (33 mg per kg) is repeated in the morning On the morning of the third day 20 cc of fluid per kg are given before 11 00 A M Urine is collected, for chemical study from 8 00 A M to 12 noon of the third day

In normal subjects the concentration of chloride in the four hour urine specimen varies from 15 to 150 mg per cent with a mean of 55 mg per cent In Addison s disease values of 225 to 360 mg per cent are commonly encountered In the presence of diabetes mellitus and in renal disease the test is of no diagnostic value The patient must be watched carefully for evidences of an impending crisis which necessitates its discontinuance

Treatment —The general care of the patient with Addison s disease is of great importance Adequate control is so difficult to attain and maintain that reference to a specialist is highly advisable Infections no matter how mild are carefully handled Excesses of physical exertion and mental strain and extremes of temperature are avoided Surgical procedures are hazardous and drugs are used with caution since untoward reactions are common A *high carbohydrate diet* protects against hypoglycemia (p 1245) and a high intake of *vitamins B and C* is indicated

Salt Therapy—The chief aim of treatment is to restore a feeling of well being and permit the patient to engage in normal activities This may be accomplished most simply, by the administration of *sodium chloride* Some patients are perfectly comfortable for fairly long periods with the

oral administration of sodium chloride in doses of 10 gm daily given as enteric coated pills

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Treatment of a Crisis—For the relief of acute adrenal insufficiency desoxycorticosterone acetate acts too slowly and large amounts of sodium

chloride and dextrose are given by continuous intravenous infusion Massive doses of desoxycorticosterone acetate (25 mg) are injected intramuscularly and 25 cc of the aqueous cortical extract are introduced subcutaneously as outlined in the following table

AN OUTLINE OF THE THERAPY OF ADRENAL CRISIS

(After Thorn and Firor)

First Day

1st 12 hours

Place the patient in a warm bed

Inject 25-35 mg of desoxycorticosterone acetate in oil intramuscularly the total quantity being divided and injected in 4 different places

Inject 25 cc of adrenal cortical extract subcutaneously in 3 divided doses

Administer intravenously by slow drip 1000 cc of 1.5 per cent NaCl solution and 1000 cc of 5 to 10 per cent glucose solution to which 25 cc of aqueous cortical extract have been added

2nd 12 hours

Slow intravenous drip of 500-1000 cc of normal saline and 1000 cc of 5 to 10 per cent glucose solution

Fruit juices and ginger ale by mouth

Second Day

Inject 10-20 mg of desoxycorticosterone acetate in oil intramuscularly

Slow intravenous drip of 1000 cc of normal saline and 1000 cc of 5 to 10 per cent glucose solution

Frequent small feedings of fruit juice dextrose tablets and candy

Third Day

Inject 5-15 mg of desoxycorticosterone acetate

Administer 3-6 gm of sodium chloride by mouth as 1 gm enteric coated salt tablets

CLINICAL DISTURBANCES OF THE ADRENAL CORTEX

The clinical disturbances of the adrenal cortex become manifest through the syndromes of *adrenal virilism* or *adrenal insufficency* In either instance the nature of the pathologic disturbance remains inferential until an exploration is made of the glandular areas

Adrenal Cortical Adenoma

Adrenal cortical adenomas develop as compensatory phenomena in conditions characterized by the destruction of the normal elements They give rise to *adrenal virilism* when clinical manifestations become apparent

Adrenal Cortical Carcinoma

The carcinoma is the most common primary neoplasm of the adrenal cortex In the *adenocarcinoma* there are columns of normal looking cortical cells and in the *carcinoma simplex* the appearance is that of a highly undifferentiated tumor containing pleomorphic and giant cells with no particular form of cellular arrangement The growths are usually yellow and vary from solid structures to multiple cystic areas They tend to invade the surrounding tissue and extend into the renal and adrenal veins Distant metastases occur in the lungs liver and bones

The malignant adrenal cortical neoplasms are usually encountered before puberty or after the age of forty In children they give rise to an *iso*

sexual precocity They may also produce *heterosexual changes* such as the masculinization of the female or the feminization of the male (p 2481) Less often the manifestations are those of *pituitary basophilism* (Cushing s syndrome) (p 1159) or a *macrogenitosoma praecox* (p 1184)

The clinical variations are probably due to the protean hormone producing capacity of the various neoplasms *Androgenic cortical tumors* are most common and they produce virilism with suppression of ovarian function in adult females Should the same condition be found in the male it results in an isosexual or true precocious puberty

Estrogenic cortical cancers are less common Should they appear before puberty in the female they lead to isosexual or true precocious puberty In young males they cause feminization with gynecomastia loss of libido and testicular atrophy

Attempts at the removal of an adrenal carcinoma are usually ineffective and the patient eventually succumbs

Metastatic Carcinoma

On rare occasions metastases to the adrenal gland are sufficiently extensive to superimpose the picture of Addison s disease on that of generalized carcinomatosis Recognition of the condition is purely academic

Adrenal Cortical Tuberculosis

See *Addison s Disease* (p 1271)

Syphilis of the Adrenal Cortex

See *Adrenal Cortical Insufficiency* (p 1271)

Friderichsen Waterhouse Syndrome

The Friderichsen Waterhouse syndrome occurs in *meningococcemia* (p 211) The manifestations are those of an *acute adrenal insufficiency* occurring during the course of a fulminating meningococcus infection

See *Meningococcus Infection* (p 208) and *Adrenal Insufficiency* (p 1271)

Hyperplasia of the Adrenal Cortex

See *Adrenal Virilism* (p 1268)

Atrophy of the Adrenal Cortex

Atrophy of the adrenal cortex may follow a *systemic infection* such as occurs in the orchitis that accompanies mumps (p 480) It may also result from changes in the controlling *anterior pituitary gland* (p 1154) In any instance the symptoms are those of an adrenal cortical insufficiency (p 1271) whose course differs from that of tuberculosis in that there is less rapid progression and a greater hope of arrest of the fundamental abnormalities

Amyloidosis and Hematochromatosis of the Adrenal Cortex

Amyloidosis and hematochromatosis involving the adrenal cortex produce the symptoms of adrenal cortical insufficiency in addition to those of the more fundamental disturbance In amyloidosis the suggestive find

ings are the *hepatosplenomegaly* and the positive *Congo red test* (p 7) In hematochromatosis the urine contains *sugar* and the *liver* is greatly enlarged See p 1076

Bilateral Adrenal Cortical Necrosis

Bilateral adrenal cortical necrosis occurs in pregnancy and causes manifestations of Addison s disease

See *Pregnancy* (p 2675)

Adrenal Cortical Hemorrhage

Extensive hemorrhage into the adrenal cortical substance occurs during *shock* (p 928) and with severe burns These facts indicate the importance of dealing with either condition in the manner of an acute crisis of *Addison s disease* (p 1271)

SΓCTION X

THE NERVOUS SYSTEM INCLUDING PSYCHIATRY

The author is indebted to

DR LEO DAVIDOFF and DR SOL W GINSBURG for invaluable criticism and advice in the preparation of this section

CHAPTER 59

INTRODUCTION

Man is distinguished from his fellow creatures by the further development of his cerebral potentialities He remembers articulates reads writes stores knowledge and reasons For these qualities as for all biological assets he pays a price If education is indeed an ornament in prosperity and a refuge in adversity it is equally true that education is the power that increases the capacity to suffer'

Whether or not it suits the practitioner s preferences he spends much of his active life dealing with functional disorders of the nervous system decidedly less often his problems involve organic neurology With due regard to the physician s needs the present section emphasizes the study of the neuroses and then deals with organic psychiatry and disturbances of the voluntary and involuntary nervous systems With deliberation the material has been written by the senior author in the belief that an exposition presented by a physician who lacks formal psychiatric training is more likely to appeal to and meet the needs of the practitioner

PSYCHIATRY

Psychiatry is the branch of the medical sciences dealing with disturbances of thought feeling and conduct It is concerned with processes that upset the mental moral behavioristic and social aspects of an individual s personality adjustments Such disturbances may affect and modify his life work and happiness or the welfare and well being of his family and associates

INCIDENCE OF PSYCHOGENIC DISTURBANCES

Each mental act is accompanied by psychic and emotional overtones of varying intensity Fear anxiety and/or apprehension accompany pain injury infection or surgical procedures no matter how trivial The ordinary mental and emotional phenomena of obvious causation offer no important clinical problem The realm of psychiatry is entered when the effect *is disproportionate* to the cause the etiology obscure or the manifestations persistent

Psychiatric disorders of sufficient intensity to warrant medical consultation are estimated to constitute 30 to 50 per cent of patient material observed in private practice More graphic and definitive evidence of the appalling incidence of mental disease is afforded by institutional figures These reveal that from 12 to 20 per cent of all patients admitted to general hospitals present conditions and problems that are primarily psychogenic approximately one person in twenty becomes a patient in a mental hospital at some time or other during his life and one individual in ten becomes more or less incapacitated by mental disease at one time or another whether or not he is hospitalized

PSYCHIATRY AND THE PRACTITIONER

In days gone by it was the clergyman whom the troubled sought in the hour of need In more recent times with the inclusion of applied psychology and psychiatry as integers in the practice of medicine psychogenic and emotional disturbances have become the province of the family doctor In the span of most lives the individual brings to his medical advisor problems of anxiety and concern relative to personal business and social adjustments, mental conflicts, sibling rivalry adolescent adjustment preoccupation with the care and rearing of children sexual difficulties marital and parental schisms, abnormal habits and disturbing proclivities and aberrations in behavior, feeling or thought Even the best integrated individual finds himself at some time or another, in conflict with himself his fellows or his community

The practitioner functions as a psychotherapist in most of the emotional and psychogenic manifestations that result from the ordinary tribulations experienced in the course of the average life Each form of therapy has an element of psychiatric guidance and the management of psychiatric disorders represents a major problem in private practice

The confidences brought from the patient to the practitioner afford an insight into character and thought processes They permit the compleat practitioner to acquire a more intelligent and rounded concept of clinical disturbances In exchange for the weary hours and tremendous energy expended in the consideration of the emotional problems of his patients the family doctor is given a panoramic view of clinical medicine that is in sharp contrast to that of the specialist whose shaft vision focuses on a field of less and less' breadth with 'more and more acuity

MISCONCEPTIONS REGARDING PSYCHIATRY

Among the many deterrents which handicap the practitioner in psychiatric guidance are the vast ignorance misinformation and repugnance of most of the population toward mental disease The very thought or statement that a person has a mental affliction stirs the animosity of patient and family Most individuals even in the group of the intelligent regard mental disease as something reprehensible and culpable Until one has had experience with a psychiatric disorder it is difficult to believe that these derangements are involuntary serious incapacitating or of major significance

It is unfortunate that many physicians share the opinions of the laity The patient who is neurotic is often stigmatized and berated or his illness is minimized and passed off with such expressions as he is just a nut' 'nothing but a neurotic or a hypochondriac or some similar derisive comment The patient is left with the impression that nothing is wrong or that his illness is imaginary or controllable at will Therapy frequently consists in such glib advice as snap out of it or you ought to be ashamed of yourself and other admonishments to the effect that the sufferer must not coddle himself and that in reality all he needs is a swift kick in the place where it will do the most good

Psychiatrists and mental hospitals are usually not rated on a much higher plane than the mental patient Most psychiatrists are regarded as being a bit on the balmy side The concept of the mental institution is

till that of Bedlam, with chains bars and walls with uniformed keepers who beat and abuse the inmates and with inhabitants who imagine they are Napoleon or the Queen of the May This popular but highly inaccurate picture is completed by the estimate of the hopelessness of prognosis since most lay persons and many physicians regard mental disease as incurable and therapeutic efforts as mere gestures except for custodial or penal care

Perhaps nowhere in the realm of medicine is there such a wide discrepancy between popular misconception and actual truth Often the practitioner functions in no more useful capacity than that of attempting the education of patient and community in the accomplishments of psychiatry

SOCIETY AND THE MENTAL PATIENT

Mental afflictions impinge upon society in respect to marriage divorce and child bearing

Marriage —It is apparent from the frequent familial occurrence of nervous and mental disturbances that marriage into a mental family is unwise and often terminates disastrously for the more normal marital partner It is not at all uncommon for the physician to be consulted by the spouse of a neurotic or psychotic patient since the afflicted has learned to live with his psychogenic complaint while the marital partner suffers inordinately Impotence in a husband produces serious symptoms in the more normal wife a frigid wife is the cause for many of the complaints of her integrated husband many persons have compulsions relative to sexual intercourse and these prove irritating and finally intolerable to the unfortunate husband or wife

Many marriages are made on a neurotic basis merely because the bride to-be bears a resemblance to the mother of the groom or the groom to the bride s father Such marriages begin unfavorably and are prone to lead to difficulties most particularly on a psychosexual basis

One of the questions most commonly asked the practitioner concerns marriage to a psychotic or a recovered psychotic patient There are unfortunately no available statistical data on this point The patient with *manic depressive psychosis* who desires to marry is warned of the risk of recurrence *Recovered schizophrenics* are advised not to marry and if they do they are urged against assuming parenthood In epilepsy it has been estimated that there is a 1 to 40 chance of epileptic offspring and the risk should be explained to the contracting parties

Regarding consanguinity the wisdom of the marriage of first cousins is often debated If there is no appreciable incidence of mental or nervous disease there would seem to be no medical objection

Pregnancy and Childbirth —Pregnancy and childbirth give rise to serious problems particularly in *epileptics* and *psychotics* This aspect has been recognized by many states where sterilization is *permitted in the* more serious psychoses

The practitioner is more commonly confronted with the problem of pregnancy in a *neurotic* This event is apt to be accompanied by *an ambivalence* in which the desire for maternity or paternity is opposed by anxieties and fears relative to the hazards of parturition The physician must take a firm stand against pressure brought upon him *to recommend*

termination of the pregnancy unless he has the fear that a psychotic epi sode is imminent Under these circumstances he is bound to consult the specialist psychiatrist before recommending a therapeutic abortion

SURGERY AND THE PATIENT WITH A MENTAL DISORDER

Surgical problems give rise to serious dilemmas in cases of neurotic or psychotic patients Diagnostic problems are considerably complicated particularly in the *conversion* and *transference neuroses* Under these cir cumstances the practitioner runs two risks which are diametrically op posed If he credits the hysterical symptom as a manifestation of a somatic disorder he may sanction or perform an unnecessary technical procedure On the other hand if he expresses too great doubt concerning the possible presence of organic disease the patient may suffer inordinately because of loss of valuable time in the execution of a necessary surgical procedure such as appendectomy or the suture of a perforated ulcer

Anesthesia gives rise to many problems in neurotics and psychotics Some demand local anesthetization in major surgery since they fear to be put asleep" Others refuse local procedures and demand inhalation anesthesia for minor procedures Exceptionally stoics refuse any anesthe sia and demand that they be permitted the masochistic pleasure of endur ing exquisite agony'

The *postoperative course* in the neurotic and psychotic is often a tre mendous problem for physician and surgeon alike Postoperative psycho ses often terminate tragically dressings are torn off catheters and tubes are pulled out and the nightmare ends with the patient leaping out of the window Oftentimes there is inordinate complaint of pain and the postoperative course is complicated by the effects of the excessive admin istration of drugs particularly the opiates which add obstipation and urinary retention to other difficulties All too frequently the neurotic pa tient will suffer from intractable vomiting paralytic ileus persistent and repeated urinary retention or a myriad of other manifestations sufficiently numerous persistent and annoying to try the patience of a saint At times it becomes necessary for the practitioner to sit down with his patient and explain that there are certain discomforts which must be endured with fortitude and courage that no further sedative medication will be ordered except for major discomfort and that unless there is more active coop eration the situation gives promise of terminating seriously if not fatally *Drug addictions* which initiate from painful illnesses are laid at the door of the physician but fundamentally they complicate a preexistent neu rosis

Conscious of these surgical difficulties the practitioner looks with dread upon surgical procedures of *election* (p 3996) particularly those which the technical enthusiasts recommend for the relief of manifestations of conversion or transference These latter include appendectomy for all manner of abdominal discomfort and correction of uterine malpositions and gynecologic reparative procedures designed for the relief of asthenia pain in the back sexual debility and the like Paradoxically in opera tions of emergency the neurotic to the astonishment and delight of all concerned often comes through with a stoicism that testifies to the rela

tive courage of these patients when faced with reality situations of con scious comprehension

THE INVOLUNTARY NERVOUS SYSTEM

The involuntary nervous system is the most vitally important and most neglected subdivision of the human mechanism Its significance rests in its widespread control of visceral hormonal and metabolic processes its neglect is due to the perfection of its mechanism inadequate anatomical representations in dissecting and operating rooms the rarity of demon strable organic disease and the difficulties of approaches to therapy

Efficiency of the Involuntary Nervous System —The efficiency of the in voluntary nervous system is one reason why its effects are so little ap preciated The physician takes for granted its near perfection just as civi lized man without due gratitude or reverence accepts the marvels of electricity radio reception and modern plumbing a switch is thrown and a bulb is expected to give out light dials are twisted and sound waves are brought in from great distances, a spigot is turned and water from a mountain side fills a bowl or bath tub Such miracles are the normal disturbances are regarded as vexatious and baffling and except for the reattachment of a loose wire or the tightening of a screw these momen tous physical phenomena are quite beyond ordinary control

Many mundane observations attest to the efficiency of the involun tary nervous system It is already functioning at birth in contrast to the tardy development of the voluntary system which is responsible for the child s being virtually helpless for the first eight to twelve months of life At the other extreme when the voluntary nervous system has ceased to function the faithfulness and hardiness of the involuntary nervous system again become manifest the vegetating moribund patient afflicted with a fatal carcinomatosis may lie comatose for days or weeks before the invol untary nervous system surrenders its last spark of vitality The voluntary nervous system is put to sleep each night while the involuntary nervous system continues its ceaseless vigil There is even the possibility that medullary centers controlled by the involuntary nervous system deter mine the sleep walker activities of the cerebrum Small wonder then that the physician takes for granted the dependability of the involuntary nervous system in the manner of his acceptance of the law of gravity

Associations and Coordinations —The major associations and coordina tions of the involuntary nervous system are not approached in their com plexity and efficiency by any piece of machinery devised by man They are not alone automatic but they are self regulating to a degree that is incomprehensible Their minor functional disturbances that enter clinical consciousness in the nature of *autonomic imbalance* (p 1395) are essen tially nuisance phenomena and only rarely incapacitating

An adequate exposition of the scope and interrelations of involuntary activities would require something more than the usual type of presen tation A satisfactory portrayal might be attempted by utilizing the con ductor s score of a great symphony In place of inscribing the notes of the scale for strings wood winds brasses and tympany the symphony of the involuntary nervous system would be scored simultaneously for the cir culatory digestive endocrine respiratory reproductive urinary and meta

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connect medulla with pons and cerebellum The principal longitudinal tracts are the pyramidal the posterior or median longitudinal bundle and the median fillet The superficial origins of the sixth to the twelfth cranial nerves originate or terminate in the substance of medulla and pons Re action patterns arising from medullary involvement appear with material on brain tumors (p 1419)

The Ventricles—The ventricles of the brain contain cerebrospinal fluid Each is lined by an ependymal membrane The four cerebral ventricles are the right and left lateral ventricles situated within the hemispheres the third ventricle between the optic thalami and the fourth ventricle in the hindbrain Each lateral ventricle is connected with the third ventricle by a foramen of Monro third and fourth ventricles are joined by the aque duct of Sylvius The fourth ventricle communicates below with the cen tral canal of the cord and with the subarachnoid spaces through the fora mina of Magendie and Luschka

Disturbances of the ventricles and their attendant reaction pictures are described with the material on hydrocephalus (p 1409) and brain tumors (p 1419)

The Spinal Cord Spinal and Cranial Nerves—The anatomic descriptions of spinal cord spinal and cranial nerves appear in the section on the per ipheral neuropathies (p 1471)

The Meninges—From within outward the structures of the voluntary nervous system are invested by pia arachnoid and dura The pia is closely attached to brain and cord and is separated from the arachnoid by the subarachnoid space in which cerebrospinal fluid circulates Arachnoid and dura are eparated by the subdural space which likewise contains cerebrospinal fluid The dura finally is separated from the periosteum of the skull or vertebrae by loose areolar tissue which further functions for the insulation of the delicate neurological structures Disturbances of the meninges are discussed in the sections on meningitis (p 1462) and in the material on vascular injuries (p 1445)

The Cerebrospinal Fluid—The cerebrospinal fluid acts as a water bed for the protection of the outer surfaces of brain and cord It flows from lateral ventricles to third and fourth ventricles through the central canal of the cord and within the subarachnoid and subdural spaces

Cerebrospinal fluid may be collected by lumbar cisternal or ventricular puncture as elsewhere described (p 3736) its physical chemical and sero logic characteristics are enumerated in the section dealing with laboratory diagnosis (p 3734)

bolic functions Beyond this the following important distinctions would prevail the harmony of the coordinating agencies would be assured by mechanisms of self regulation there would be no rests intermissions or intervals, provisions would be available for tightening loosening and replacing strings without interruption of the performance and the maestro would be invisible

THE VOLUNTARY NERVOUS SYSTEM

The voluntary nervous system is mainly concerned with the relationship of the individual to his external environment The spinal cord with its spinal nerves has motor and sensory functions The brain is the seat of consciousness and memory, it contains the receptive nuclei for sensory impulses which come from skin joints muscles and organs of special sense it may originate motion and control or coordinate the actions of muscles which are primarily innervated by cells in the spinal cord and the lower brain centers The brain has the faculty of correlating the knowledge which is acquired by experience and of utilizing these deductions for synthetic mental processes

The component parts of the brain are the cerebral hemispheres mid brain cerebellum pons varolii and medulla oblongata

The Cerebral Hemispheres—The cerebral hemispheres are of large size they exhibit a high degree of specialization with regard to function the reaction patterns produced by localized lesions are discussed in greater detail in the consideration of *neoplasms of the brain* (p 1423) and *vascular accidents* (p 1439) The cerebral hemispheres are connected by the corpus callosum which functions for the coordination of right and left subdivisions

Midbrain—The midbrain connects those portions of nerve tissue below tentorium cerebelli and cerebral hemispheres It is traversed by the aqueduct of Sylvius and contains structures concerned with visual oculomotor auditory, painful and caloric sensations as well as the nuclei and roots of origin of the third fourth and part of the fifth cranial nerves The reaction patterns' of midbrain injuries are discussed in the section on *cerebral neoplasms* (p 1423)

Cerebellum—The cerebellum has a central vermis and two lateral hemispheres Each hemisphere is connected with the brain stem by inferior middle and superior peduncles The cerebellum correlates sensory impulses from the internal ear muscles and other organs The reaction patterns resulting from cerebellar injury are discussed in the paragraphs on *brain tumors* (p 1423)

Pons Varolii—The pons varolii lies between midbrain and medulla it forms a bridge which connects the two cerebellar hemispheres and its posterior surface forms the upper half of the floor of the fourth ventricle It contains nuclei of origin or termination of the fifth sixth seventh and eight cranial nerves Disturbances of the pons Varolii give rise to characteristic reaction patterns described in the section on *brain tumors* (p 1423)

The Medulla Oblongata—The medulla oblongata is a direct continuation upward of the spinal cord It contains important and vital cardiac vasomotor and respiratory centers Longitudinal bundles of nerve fibers

toire of five or six words bladder and rectal control are complete and the hours of sleep have been reduced from 20 per day at six months to perhaps 13 the cup is used for drink ing purposes and a spoon for the ingestion of soft foods

By the second birthday the child can run and is able to combine words into phrases *its coordination is sufficient to permit it to throw a ball and make an effort at catch*

At *three years* of age the child has advanced to the stage where it assists in dressing and may even put on its own shoes It recognizes the obvious portions of its anatomy such as the eyes nose and mouth and points them out in the mirror or in pictures It begins to repeat sentences and numerals and recognizes and enunciates its own name

At the age of *four* the child knows its sex recognizes common objects and may be sent on errands in and around the house At *five* it is able simultaneously to carry out several commissions draws and copies in the familiar picture books and is able to dress and undress without assistance

At *six* the child knows the time of the day recognizes pictures that are attractive and distinguishes those that are ugly appreciates the difference between the right and left hands and is able to count through the teens He describes pictures of familiar objects, names the colors and the days of the week and begins to recognize the rights of other members of the household

School Age to Adolescence.—From school age until adolescence the development and mental progress of the child are best estimated by the *scholastic standing* The school record *reflects* the child's intellectual capacity and behavior and his ability to cooperate and play with contemporaries of both sexes

Girls develop *secondary sex characteristics* at the age of from seven to ten and the menarche occurs on or about the age of thirteen Boys lag somewhat behind in maturation and their masculine hairiness and manly voice do not become apparent until the twelfth to sixteenth years

Without the aid of complicated and intricate tests (q v) the practitioner recognizes which of "his children" are developing normally in school in extrascholastic activities and in the business of adaptation to the science of living He has no difficulty *in noting* the backward the maladjusted misfits and unhappy youngsters Without much formality he usually has a clear picture of the etiology of the disturbance whether organic character ologic or situational—in the latter instance most likely due to parental ignorance or misfortune See *Mental Deficiency (Feeblemindedness)* (p 129)

The Normal Adult Personality and Behavior Patterns.—The concept of the normal adult is purely relative and cannot be defined with rigidity Normality varies in different cultures and at different levels of economic and social integration Mutations occur with the sex and age of the person and the position in life

It is accordingly difficult to catalogue and analyze the normal personality and behavior *patterns* as they are observed in clinical practice Each practitioner is well acquainted with the customs and habits in his own community and recognizes deviations therefrom Aberrations require definition for diagnostic prognostic and therapeutic purposes A child or an adult may prove to be backward or recalcitrant through no conscious desire to be difficult but as the result of mental deficiency impaired perception a defect in hearing or vision and through inattentiveness or speech impairment. The practitioner *attempts to analyze* psychic and emotional aberrations in much the same manner as disturbances in respiration or circulation

The ingredients that enter into personality behavior patterns and conduct include *mentality perception attention consciousness thought production thought progression orientation judgment memory* and *effects* Variations and disturbances may be *reflected in total personality or character alimentary or sexual appetite* and *behavior sleep visceral function motor behavior speech* or *posture* Each of these elements is defined and the disturbances catalogued in the material that follows

The "Normal" or Integrated Personality—

1 The normal individual is capable of achieving a feeling of self security and self esteem without exaggeration in either direction

2 He is able to work fruitfully at his given occupation and derive *satisfaction from it* *He* progresses with time to gain a satisfactory reward both economically and otherwise

3 He is able to maintain a pleasant and adequate relationship *with his colleagues*

4 He is able to give and accept love from a suitable partner and to have satisfactory sexual relationship with his mate

CHAPTER 60

PSYCHIATRY: NORMAL AND ABNORMAL MENTAL AND EMOTIONAL DEVELOPMENT

NORMAL MENTAL AND EMOTIONAL DEVELOPMENT

AN UNDERSTANDING of the variations that come into the realm of psychiatry requires a prior knowledge of the normal development and range of the intelligence and emotions. Mental aberrations and afflictions then become clearer as variants of the normal rather than processes which arise without meaning or reason.

The development of the human mind and character provides a fascinating spectacle with infinite variations on the theme of human metamorphosis. Although the definition of the normal is broad and loose, some generalities are recognized in attempts to appreciate conditions of arrested development, regression and deterioration.

At Birth and First Year.—*At birth* the child is capable of moving its hands and feet; it is frightened by sudden loud noises; it detects the odor of milk, makes its way to the source and suckles the maternal breast or the rubber nipple. It resists restraint and withdraws the part that is exposed to painful stimulus.

By the end of a month the child blinks when startled. It follows familiar objects with its eyes and *in another month apparently recognizes familiar objects such as the bottle* and familiar faces, particularly of its mother. *At four months* it reaches for the familiar object and apparently recognizes voices. *By the seventh month* it sits erect with slight support, vocalizes syllables and makes crowing sounds. *By the tenth month* the child sits alone and says "mama" or "dada" and perhaps learns a simple nursery trick such as shaking "bye bye." *At the end of a year* the child walks with some assistance and is able to say *one or two words*. It begins to have an idea of obedience and should have learned sphincteric control of bladder and rectum.

Pre-school Age.—*At a year-and-a-half* the child is able to climb stairs and has a reper

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2 He is able to work fruitfully at his given occupation and derive satisfaction from it He progresses with time to gain a satisfactory reward both economically and otherwise

3 He is able to maintain a pleasant and adequate relationship with his colleagues

4 He is able to give and accept love from a suitable partner and to have satisfactory sexual relationship with his mate

5 He has intimate friends of the same sex
6 He enjoys a gratifying avocation such as a sport or hobby
7 He is capable of a certain amount of self-criticism and self-examination He sets neither too high standards for his station in life nor is he too compulsive in his own behavior
8 He is able to confront himself with his own inadequacy and transgressions without excessive anxiety or approach
9 He is ambitious but not excessively so His ambition is not such as to turn each failure into a tragedy or to compel him to make a virtue of necessity
10 He is able to take orders from superiors and give them to inferiors—in either case without hostility or resentment
11 He is able to withstand without excessive anxiety a fair amount of deprivation and loss
12 He performs his excretory functions without guilt or anxiety

ABNORMAL MENTAL AND EMOTIONAL REACTIONS

"All the world is queer save thee and me
And even thou art a little queer
Robert Owen (1771–1858)

The broad concepts of normal behavior and mental and emotional reactions add to the difficulty of defining what is abnormal The practitioner recognizes two guiding principles in his evaluation of patients with aberrations of behavior

1 The abnormal represents a *quantitative variation* from the normal
2 The borderline between normality and the abnormal is crossed when the patient suffers *interference* with life-work, companionship or the pursuit of happiness as the result of excessive or protracted mental or emotional disturbance

Mentality

The mentality of a patient reflects intellectual capacity It is independent of knowledge or education since many savants and pedants are psychopathic while illiterates may have a rich potential mental capacity See *Psychometric Tests* (p 1325)

Amentia —Amentia signifies an innate mental deficiency or a confusional psychotic state bordering on stupor and characterized by clouding of the sensorium difficulty in grasp and retention and disorientation Because of the confusion in the varying uses of this term it is best avoided

Dementia —Dementia is a blunting or restriction of mental activities and capacities There is usually growing incapacity for appreciation and learning memory is defective and confusion may exist It is increasingly difficult for ideas to penetrate and judgments to be formed especially in moral and aesthetic spheres

Feeblemindedness —Mental deficiency is usually considered present in any individual whose intelligence quotient is below 70 The grades of feeblemindedness range from idiocy through imbecility to moronity See p 133

Perception

Perception is that mental function by virtue of which impressions made upon the sensory organs are received and identified understood or interpreted in consciousness Normally a nervous impulse produces visual auditory or other sensory images which the individual recognizes and interprets in the light of experience

Hallucination—Hallucination is an imaginary sensation usually referred to the senses of hearing sight or smell Auditory hallucinations are most commonly encountered The hallucination is a normal function in dream life

Although imaginary hallucinated material is a real part of the patient s mental life and expresses unconscious material which has broken into consciousness The material of the hallucinatory experience expresses basic emotional needs such as self criticism and punishment substitutions for love or deprivation of love or enhancement of self esteem Hallucinations are found in many serious psychoses such as *manic depressive* or *schizophrenic reactions* and in organic delirium They are absent in the neuroses

Illusion—Illusions are perceptual misinterpretations Objects are perceived not as they are but in a distorted and changed form Even in normal people on tense occasions a perception may be distorted and any figure appears to be a loved one eagerly awaited or a feared person observed with dread In normal people cortical judgment and other senses quickly correct the misinterpretations

The elements likely to lead to illusions are deeply intense affective states ardent wishes or strongly urgent drives and impulses Illusions occur in *toxic states deliria* and in the *psychoses*

CONSCIOUSNESS

Consciousness represents that part of the mental life of which an individual is aware at any given time It constitutes a much smaller part of our mental life than is usually recognized By some it is considered almost infinitely small as compared to the preconscious and the unconscious

Absence of Consciousness—Loss of consciousness usually fleeting is seen in *hysterical attacks* in *syncope* and following *head trauma*

Clouding of Consciousness—Clouding of consciousness is a state in which the environment is not clearly perceived The patient is in a mental fog which may be very difficult to pierce Sensory stimuli which ordinarily would call forth a response fail of apprehension Clouding of consciousness may become so pronounced as to develop into somnolence or even stupor The condition is found commonly in association with long debilitating physical illness and may be seen in functional disorders such as *hysteria*

Confusion.—Confusion is characterized by bewilderment perplexity impairment of the sensorium difficulty of grasp disorientation or poverty of ideas It occurs largely in acute mental conditions of toxic infectious or traumatic nature in *manic depressive psychoses* and *schizophrenia*

Delirium—Delirium is the syndrome characterized by restlessness clouding of consciousness disorientation visual and auditory hallucinations confusion dream like thinking and illusions It may be accompanied by anxiety and uncertainty It is usually associated with *toxic infectious illness* and is commonly of short duration On recovery there remains no memory or only patchy remembrance of what transpired

Low grade deliria are often overlooked particularly in *post operative states* In these there is relatively slight affective disturbance and the patient responds to the stimulus of the doctor s presence by rousing himself to momentary clarity Similar states are occasionally found in *hysteria*

Depressive trends in deliria often end in *suicide* *paranoid delina* may progress to permanent psychotic states

DIFFERENTIAL DIAGNOSIS OF

States of Coma and Unconsciousness

Coma and unconsciousness are characterized by impairment of the capacities to receive or respond to stimuli In profound states reflexes are absent and sphincteric control is lost. Coma may develop suddenly or it may follow gradually upon increasing drowsiness and somnolence

CAUSE	DIAGNOSTIC FEATURES
Cardiovascular Disorders (Generalized)	Forward and backward failure (pp 920 941) Acute coronary insufficiency and thrombosis (p 983) Complete heart block (p. 879) Hypertensive toxemia of pregnancy (p 2038) and malignant hypertension (p 916) Define physiologic derangement for therapeutic indications
Drugs Poisons and Physical Agents	Alcoholism Sedatives and hypnotics particularly barbiturates chloral and bromides Opiates general anesthetics and overdosage with insulin (p 1241) Encephalopathies of arsenical and sulfonamide poisoning Asphyxia with carbon monoxide and other poisonous gases Sunstroke and exposure—particularly freezing
Infection (General)	Nonspecific terminal event in overwhelming infections Particularly in weakened and debilitated patients infancy and old age
Metabolic Disturbances	Profound cachexias associated with chronic disease and malignancy Hypoglycemia and diabetic acidosis Uremia azotemia and renal insufficiency Cholemia as in acute yellow atrophy of the liver Thyrotoxic crises and adrenal cortical deficiency Get urinalysis and blood chemical studies (pp 3066 3712)
Neurogenic	Increased intracranial tension from trauma, fracture of skull brain tumor brain abscess or hydrocephalus Encephalitides meningitides poliomyelitis or general paresis Cerebro-vascular accidents such as hemorrhage embolization and thrombosis Epilepsy Supplement neurologic status with spinal fluid examinations radiography electro-encephalography and specialist consultation
Psychogenic	Hysteria (p 1353) schizophrenia (p 1364) and manic-depressive states (p 1368)
Traumatic	Open and closed injuries of the skull Fractures and internal hemorrhage particularly of middle meningeal artery (p 1453) Severe burns Massive exsanguination from any portion of the body

Dream States —Dream states are periods of consciousness in which perception of environment is dulled and confused and in which hallucinatory

experiences are common On restoration of normal consciousness the patient has little or no recollection of what has transpired and may often volunteer the statement It was like a dream These disturbances may merge with deliria fugue states or dissociation of personality They occur in affective disorders such as *hysteria* and in *epilepsy*

Stupor—The term stupor as used in psychiatry may imply (*1*) a state of unconsciousness usually due to *organic conditions* in which speech and motor reactions are absent or (*2*) a seeming state of unconsciousness in which thought *is active* intellectual and sensorial clarity are present but the patient remains mute and motor activity is suspended The latter is psychogenic and seen in *depressions* and *hysteria* In this sense it is used almost synonymously with mutism

Catatonic stupor is a variant of schizophrenia characterized by catatonia mutism negativism hypersuggestibility and catalepsy

Coma—Coma is total loss of consciousness with absence of all voluntary motion

Emergency Treatment—The treatment of coma cannot be carried out with intelligence until the causative factor is elucidated Meantime emergency measures are practiced for the preservation of life as summarized below

1 Control obvious hemorrhage
2 Clear airway and administer artificial respiration (p 3766) If necessary send for pulmotor
3 Transport to hospital as soon as condition permits
4 If blood pressure is excessive prepare for phlebotomy (p 3780)
5 If blood pressure is at shock level bandage three extremities and set up intravenous drip with dextrose and saline plasma or whole blood as indicated (p 3775)
6 If urine contains acetone substitute sodium r lactate or Hartmann s solution in infusate
7 If blood sugar is low substitute 10 to 50 per cent dextrose in infusate
8 If catheterized urine contains *sugar* add insulin and dextrose to infusate
9 In suspected poisonings lavage stomach as soon as possible
10 With bitten tongue and history of epilepsy follow principle of skilful neglect
11 With evidences of congestive failure consider digitalization (p 858) and phlebotomy (p 3780)
12 In suspected adrenal cortical deficiency add hypertonic saline to infusate
13 In thyrotoxic crises add iodide to infusate
14 With impaired respiration cyanosis and backward or forward failure prepare for oxygen therapy (p 3827)
15 If spinal fluid is under increased tension bloody or xanthochromic summon the neurosurgeon after obtaining radiographs of the skull (p 1450) Examine fundi for evidences of papilledema (p 1578)
16 If spinal fluid is turbid temperature is elevated or leukocytosis is

Depressive trends in deliria often end in *suicide* *paranoid deliria* may progress to permanent psychotic states

DIFFERENTIAL DIAGNOSIS OF

States of Coma and Unconsciousness

Coma and unconsciousness are characterized by impairment of the capacities to receive or respond to stimuli In profound states reflexes are absent and sphincteric control is lost. Coma may develop suddenly or it may follow gradually upon increasing drowsiness and somnolence

CAUSE	DIAGNOSTIC FEATURES
Cardiovascular Disorders (Generalized)	Forward and backward failure (pp 920 941) Acute coronary insufficiency and thrombosis (p 983) Complete heart block (p 879) Hypertensive toxemia of pregnancy (p 2638) and malignant hypertension (p 916) Define physiologic derangement for therapeutic indications
Drugs Poisons and Physical Agents	Alcoholism Sedatives and hypnotics, particularly barbiturates chloral and bromides Opiates general anesthetics and overdosage with insulin (p 1241) Encephalopathies of arsenical and sulfonamide poisoning Asphyxia with carbon monoxide and other poisonous gases Sunstroke and exposure—particularly freezing
Infection (General)	Nonspecific terminal event in overwhelming infections Particularly in weakened and debilitated patients infancy and old age
Metabolic Disturbances	Profound cachexias associated with chronic disease and malignancy Hypoglycemia and diabetic acidosis Uremia azotemia and renal insufficiency Cholemia as in acute yellow atrophy of the liver Thyrotoxic crises and adrenal cortical deficiency Get urinalysis and blood chemical studies (pp 3666 3712)
Neurogenic	Increased intracranial tension from trauma fracture of skull brain tumor brain abscess or hydrocephalus Encephalitides meningitides poliomyelitis or general paresis. Cerebro vascular accidents such as hemorrhage embolization and thrombosis Epilepsy Supplement neurologic status with spinal fluid examinations radiography electro-encephalography and specialist consultation.
Psychogenic	Hysteria (p 1353) schizophrenia (p 1364) and manic-depressive states (p 1368)
Traumatic	Open and closed injuries of the skull Fractures and internal hemorrhage particularly of middle meningeal artery (p 1453) Severe burns Massive exsanguination from any portion of the body

Dream States —Dream states are periods of consciousness in which perception of environment is dulled and confused and in which hallucinatory

Hypochondriasis —Hypochondriasis is a state of morbid anxiety about health and is usually associated with a false belief that an organ is organically diseased It may be met in *depressed states schizophrenia involutional melancholia* and other psychoses It appears also as a *neurotic manifestation* in terms of a profound unconscious drive such as narcissistic preoccupation or masochistic expiation of guilt

The difference between hypochondria as it occurs in the psychoses and that which is encountered in the neuroses lies in the comparative severity of the underlying disturbance rather than any qualitative difference in the unconscious mechanisms Hypochondriacal preoccupation may occur in a psychotic setting or in a simple neurosis If the disturbance is particularly rigid if there is any tendency to systematization or the hypochondriacal notions become queer and distorted a schizophrenic or paranoic psychosis should be suspected

Ideas of Reference —Ideas of reference are morbid ideas that actions words and mannerisms are directed or referred to oneself they occur in *schizophrenia* and *paranoia* and may be as obstinate as delusions

Overdetermined Ideas —Overdetermined ideas are those which have multiple determinants They are anchored to many aspects of the patient s life and personality and are particularly resistant to treatment

Trend — Trend in psychiatry refers to the ideational content of any clinical syndrome A patient is said to have a homosexual trend not by virtue of his actions and feelings but by virtue of a constellation of ideas relating to homosexuality (Hinsie and Shatzky)

Progression of Thought

Progression of thought normally flows in logical sequence toward a definite conscious end There should be in the stream of thought an orderly sequence of more or less obviously related ideas passing uninterruptedly and without digression from an initial to a goal idea

Blocking —Blocking is a disturbance in the flow of thought in which expression and progression of thought suddenly cease Blocking is due to the activity or revival of a thought or complex with a powerful unpleasant affect It may result in a total obstruction of speech In some degree blocking is a universal phenomenon When it becomes a predominant obstacle to thought it characterizes *schizophrenia*

Circumstantiality —Circumstantiality is a disturbance in the flow of thought in which the goal idea is reached only after relating a mass of irrelevant and unimportant details and incidents It is characteristic of persons who cannot distinguish essentials from non essentials and who cannot maintain a sharply focused concept of what it is they wish to say It is found most commonly in the *feebleminded epileptics senile psychotics* and in *manic states*

Clang Association —Clang association is an association based on the similarity of the sound of words with no regard to the dissimilarity of ideas It is found in flight of ideas

Flight of Ideas —Flight of ideas is a disturbance of the train of thought in which the goal idea is never reached because of frequent digressions related or not It is as though thinking went on too quickly and no idea was ever completed The association of ideas may be through a chance

pronounced inaugurate massive antibiotic therapy by intravenous and intrathecal injections of penicillin (p 106)

17 Even if breath gives evidence of ingestion of alcohol remember that the intoxicated patient is subject to the same disturbances as his sober fellow citizen furthermore the drink may have been given for the relief of the very symptoms which later terminated in coma

Attention

Attention is the application of energy in the sphere of consciousness by the individual aware of the application of energy One should not speak of attention when the mind functions without the overt knowledge of the subject (Hinsie and Shatzky)

Aprosexia —Aprosexia is the inability to maintain attention It may be due to preoccupation with one s own thoughts and problems or may exist as a form of negativism Aprosexia may be selective for certain subjects

Blunting of Attention —Blunting of attention is an extreme form of inattention It is usually found in *stupor* and *coma* when painful stimuli fail to arouse the patient s attention

Distractibility —Distractibility is a state in which attention passes rapidly from one subject to another and the patient gives notice to every passing stimulus It occurs in *mania delirio* and *flight of ideas*

Fluctuation of Attention —Fluctuation of attention is the condition in which the attention varies more easily and to a greater extent than normal It is met in *organic syndromes* and *delirio*

Rational Thought (Production of Thought)

Rational thought is that thought directed by, and taking place in conscious awareness

Autism —Autism is characterized by the fact that it is uncontrolled by conscious awareness and experience it rarely leads to action and fails to take the facts of reality into consideration It is most marked in *schizophrenia* where mental activity may be completely independent of the ordinary realities of life

Delusions —Delusions are false beliefs which are not susceptible to the ordinary processes of logic or reasoning which are out of keeping with a person s education and background and which arise in response to definite unconscious emotional needs of the patient In other words the difficulty in the delusional patient is not really as it might seem in the field of thinking but in the emotional life Delusions are of many types such as delusions of persecution of grandeur of self accusation or of poverty

The delusions are reactions to highly painful affective or instinctual demands with which the patient is unable to deal adequately They may be compensatory for a painful failure or a profound sense of inadequacy or inferiority they may be projections of unconscious instinctual demands which the patient cannot tolerate because of a great sense of guilt Delusions are encountered in many mental disorders such as *schizophrenia* and *paranoia*

amnesia usually develops which may involve memory for events near the time of the treatment

Hysterical amnesia may relate to a circumscribed series of events in the patient's life usually associated with severe emotional conflict It may involve memory for all events up to a relatively recent (traumatic) point as in the *war hysterias*

Retrograde Amnesia —Retrograde amnesia involves events antedating the onset of the amnesia proper It may be seen in *head injuries* and *epilepsy* or it may be psychogenic

Anterograde Amnesia —Anterograde amnesia includes material subsequent to the onset of amnesia It is common in *senile psychoses* and after head injuries

Confabulation —Confabulation is the process by which the patient fills in gaps in his memory by falsification which he in turn accepts as actual The confabulations are easily suggested and may be directed by the person to whom they are narrated They are found in *Korsakoff's syndrome* and the *senile psychoses*

Déjà Vu —Deja vu is the illusion of memory in which there is a feeling of familiarity on seeing a new object or scene of which there has been no previous observation Likewise there may be the feeling that a new experience has been encountered before

Jamais Vu —Jamais vu is the phenomenon in which familiar objects or experiences occasion the illusory feeling of newness or unfamiliarity Both deja and jamais vu are seen in *normal states* as well as in *epilepsy acute intoxication schizophrenia* and *hysteria*

Hypermnesia —Hypermnesia is an exaggerated activity of memory seen in excited states especially *manic reaction* and occasionally in *paranoia* It is usually limited to certain periods and events which are recalled with great vividness and intensity and in extraordinary detail It can be induced under *hypnosis*

Paramnesia —Paramnesia is falsification of memory and includes confabulation and retrospective falsification It is observed commonly in *Korsakoff's syndrome* and the *senile psychoses*

Retrospective Falsification —Retrospective falsification and illusions of memory are created by the patient to satisfy unconscious needs to embroider or distort the truth or accuracy of memory In the *paranoid psychoses* they may be used to create supporting evidence for a delusion

PERSONALITY

Personality represents the habitual pattern of behavior of the individual in terms of physical and mental activities and attitudes particularly as these have social connotations (Healy Bronner and Bowers)

Depersonalization —Depersonalization is the feeling that one is changed from what one previously was and that one's own personality has lost its identity The patient feels as though he were dead or that there is no world in which he truly exists Reality may lose its character and the environment assumes an unreal quality Depersonalization phenomena are found in *schizophrenia* and as infrequent manifestations of a profound *neurosis*

Dissociation (Double Personality) —Dissociation is the phenomenon in

stimulus from the environment through irrelevant memories or through clang association It is found in states of *manic excitement*

Neologisms —Neologisms are words or phrases coined by the patient They are frequently condensations of several words or symbolizations of unconscious material and are found in *schizophrenia*

Obsessive Thinking —An obsession is a persistently recurring and distressing thought upon which attention must be focused even though it is adequately evaluated by the intellect and stopped by the will (Maslow Mittleman) An obsession is not consciously influenced by logic reasoning or judgment

Perseveration —Perseveration is an organic phenomenon in which an echoing lag makes it impossible for the patient to keep up with changing topics An *arteriosclerotic* for example may say correctly that he is fifty six years old and then answer that he was married fifty six years and was born in 1856

Retardation —The slowing of the initiation and movement of thought is termed 'retardation The patient may complain that he thinks and speaks more slowly It is seen characteristically in the *depressed* and in *schizophrenics* during phases of depression

ORIENTATION

Orientation is an awareness of relationship to place time and persons

Disorientation —Disorientation is the inability to estimate correctly the time place or persons in an environment It may occur in any mental disease in which there is extensive impairment of memory attention or perception It is commonly found in *acute toxic states* and *organic psychoses*

JUDGMENT

Judgment is the ability to recognize the true relation of ideas and appraise their relative merits importance and significance

Lack of Insight —Insight indicates an awareness of illness and an appreciation of underlying mechanisms Lack of insight occurs in *hypochondria hysteria* and the *psychotic states*

MEMORY

Memory is the process whereby data acquired and presented to consciousne s are stored later to be summoned and again presented to consciousness Even the simplest act of memory involves fixation of an impression its consideration and its subsequent recall

Agnosia —Agnosia in psychiatry is loss or disuse of knowledge of objects It is caused by emotional forces and is not associated with loss of sensation or mental deterioration

Amnesia —Amnesia is absence of memory It may be complete or partial, continuous periodic or circumscribed organic or functional

Characteristic of *senile deterioration* or *dementia* is the failure of memory for recent events with retention of memory for remote events This may progress until almost complete loss of memory is encountered In *cerebral arteriosclerosis* a more patchy but similar loss of memory is found

After convulsive therapy especially when *electric shock* is utilized an

us fears what cannot be consciously acknowledged or what is desired but which bears too great a burden of guilt for conscious recognition

Anxiety is used in contradistinction to *apprehension* which is an anticipatory dread of something that may be about to happen

Phobias—Phobias are morbid fears precipitated by the presence of some harmless or indifferent object or situation The fear arises from factors deep in the patient s unconscious the objects which explode the fear are not what is actually dreaded but are substitutes or symbols for ideas which would be even more painful In reality the fear arises from unconscious forces within the patient s mind and these are merely represented by the external object or situation which precipitates the terror

Phobias are encountered in the *neuroses* especially *psychasthenia* They may exist for anything A list of some of the more common phobias is appended

Acarophobia—The fear that mites or minute worms infest the skin
Acrophobia—Morbid fear of being on high places or aloft in the air
Agoraphobia—Morbid anxiety when in open spaces
Anthropophobia—Fear of men
Autophobia—Morbid fear of being alone
Cancerophobia—Morbid fear of having cancer
Claustrophobia—Morbid anxiety when in narrow or enclosed spaces
Coprophobia—Morbid repugnance to filth as in defecation
Erythrophobia—Morbid fear of blushing or of exhibiting diffidence or embarrassment
Galeophobia—Morbid fear of cats
Goiterophobia—Fear of goiter
Gynephobia—Fear of women or aversion to their company
Hemophobia—Morbid dread of seeing blood Illness such as fainting at the sight of blood
Mysophobia—Morbid fear of contamination or dirt
Necrophobia—Morbid fear of dead bodies
Nyctophobia—Morbid fear of darkness
Ochlophobia—Morbid fear of being in crowds or groups of people or in crowded places
Phobophobia—Fear of fear
Pyrophobia—Morbid anxiety about fire
Scotophobia—Morbid dread of darkness (blindness)
Syphilophobia—Morbid dread of contracting syphilis Delusional belief of having the disease
Xenophobia—Anxiety or fear in presence of strangers
Zoophobia—Morbid fear of animals especially domestic animals
See also *Phobias* (p 130)

Apathy—Emotional dulling and inadequate emotional reactions to situations ordinarily giving pleasure or pain characterize apathy Apathy may result in total disinterest in the environment or the patient s own condition and lack of contact with reality

Cyclothymia—Cyclothymia refers to fluctuations characterized by alternation of optimism and pessimism cheerfulness and sadness pep and the blues In these the mood is not adequately motivated in reality and cyclothymia reaches its full development in the *manic depressive psychosis*

Depression—Defection of mind varying from feeling blue to utter despondency is depression It may be considered pathological when it is unoccasioned by external circumstances or when it is too profound or long lasting in relation to the nominal cause

Euphoria Elation Exaltation Ecstasy—*Euphoria* is an exaggerated feeling

which part of the personality becomes split off and is not available to conscious control Relatively simple examples are seen in somnambulism automatic behavior or fugues

Dissociation means many things to many people The term has been used for the vertical splits which characterize multiple personalities (*Dr Jekyll and Mr Hyde*) It has also been used to denote dissociation of different aspects of psychological functions as the dissociation between thinking and feeling which Bleuler believed the underlying disturbance in schizophrenia, it has been used for many other segmentations of mental processes such as are encountered in psychosomatic phenomena hysterical amnesia or hysterical palsy

Perhaps the best general significance to apply to dissociation would be that of any tendency to split up or fragment any aspect of the psychological functions whether the fragmentation be in a horizontal or vertical layer or piece by piece

AFFECT

Affect is ordinarily used as a synonym for emotion though it has much more definite implications of special importance in psychiatry From that viewpoint it is best defined as a feeling tone a pain pleasure accompaniment of an idea or mental representation (Healy Bronner and Bowers)

The affect (emotion) normally varies with the external environment the state of health and the position of the individual in reality The normal person s mood is expected to reflect *the total situation* In times of stress or following a great loss a mood of depression may be considered quite normal Following a high achievement a recent promotion or on a festive occasion elation normally is expected The reaction should be fitting and commensurate to the stimulus producing it neither too profound nor too lasting *Charged stimuli* are those capable of affect productions

Abnormal disturbances in affect are those motivated by forces of which the patient is unconscious and which are beyond the control of intelligence reason and conscious deliberation

Agitation—Agitation which occurs mainly in patients suffering from certain forms of *depression* or *involutional melancholia* is a state of increased activity It may range from mild restlessness to incessant overactivity usually in motor behavior

Ambivalence—Ambivalence is a state of conflict in which opposite feelings are noted toward the same person at the same time as love and hatred of a parent by a child The individual may be conscious or unconscious of the feelings and hence of the conflicts growing from them

Anxiety—Anxiety is fear in the absence of actual danger *i e* fear occasioned by inner psychic forces of which the person is unconscious It is associated with a feeling of dread which may be related to a definite circumstance such as illness or may be entirely beyond the patient s capacity to define (I do not know myself what it is I am afraid of) It is often accompanied by the physical manifestations such as tachycardia pallor and sweating

The deep underlying tides of unconscious terror are causative forces in the production of neuroses and are to be differentiated from symptomatic fear Fear in the psychological sense represents a defense Each of

us fears what cannot be consciously acknowledged or what is desired but which bears too great a burden of guilt for conscious recognition

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of well being often in sharp contrast to the reality situation It is a milder expression of the types of enjoyable feeling, confidence and sense of well being and capacity known as *elation* The latter may be very transient and quickly followed by an angry irritation A still more intense expression of these feelings is found in *exaltation* where the attitude is that of grandeur and all the reactions are exaggerated to the extreme A related but somewhat different disturbance of mood is found in *ecstasy* Here a quiet sense of peace and well being is practically always associated with deep religious conviction The patient feels beyond (really above) mundane activities and the difficulties of man as though he had been reborn

'Philes —'Philes represent unusual attachments beyond reason The necrophile is inordinately concerned with death, the bibliophile with books The list of the phobias may be paralleled by the philes

Panic — Panic is not merely a high degree of fear, but a fear based on prolonged tension with a sudden climax which is characterized by extreme insecurity suspiciousness and a tendency to projection and disorganization" (Diethelm) Severe paroxysms of panic are prognostically more serious than anxieties and may herald an approaching schizophrenic illness For instance homosexual tendencies which give rise to long standing conflict and tension not infrequently result in panic

Tension —Tension like anxiety and fear may be conscious or unconscious It is a state of mind induced by conflict and is characteristic of the *neuroses* The struggles often entirely unconscious produce a feeling of strain and tautness apparent in the ' tense facial expression A tense person is tight fidgety restless tremulous a chain smoker, and the like

Appetite

Appetite is a natural longing or desire it usually refers to food but may be applied to learning sex or music

Anorexia —Anorexia is loss of appetite A distinction is made between true anorexia nervosa and the anorexia due to distorted ideas about the stomach and intestinal tract or delusions about food See p 1768

Bulimia —Bulimia is excessive insatiable appetite It is encountered as a compulsive manifestation and may occur after head injuries or encephalitis as well as in *hysteria* Obstinate bulimia may lead to obesity (p 695)

Morbid Hunger —Morbid desires for food are found in various emotional and mental disorders, such as *anxiety states compulsion neuroses* and *schizophrenia*

Eating may be utilized as an instrument to allay anxiety and tension and in response to a craving that is only vaguely associated in consciousness with ordinary hunger

Sexual Behavior

Normal sexual function in the adult includes much more than the genital aspects of intercourse A well integrated sexual relationship embraces genuine feelings of love for a partner of the opposite sex the desire to engage in the sexual act with that person the capacity to perform the act with resultant orgasm for each a post coital feeling of release and gratification and a capacity to relax and fall asleep There should be adequate awareness of the partner s moods and sexual needs feelings of ten

derness the necessary preliminary foreplay without revulsion or fright and a capacity for release in action and language The estimate of what constitutes a normal and adequate sexual relationship is complicated by social economic and emotional factors as well as conscious and unconscious attitudes It can be estimated only by a thorough investigation of sexual functioning and total personality

A man may be genitally adequate and capable of erection and orgasm and yet not be healthy sexually he may be unable to form any attachment for a woman he may need to use prostitutes exclusively he may need to escape immediately after completion of the sexual act intercourse may be possible only after drinking or there may be post-coital restlessness and irritability

Women have parallel difficulties they may be incapable of ardor or orgasm the climax may be premature or delayed they may be inconstant in their male attachments or they may require masturbation prior to intercourse or preliminary alcoholism Any of these manifestations of emotional difficulty point to a profound unconscious conflict which may produce evidences in a host of ways seemingly unrelated to the sexual life

Exhibitionism —Exhibitionism is the need to display the body its parts or sexual activities in order to arouse sexual interest or to compensate for unconscious feelings of sexual inadequacy or impotence

Fetishism —Fetishism is erotic gratification through the use of a fetish such as an article of clothing or some nongenital portion of the body The object arouses erotic impulses usually through unconscious associations

Homosexuality —Homosexuality is the love for a person of the same sex In the form of interest as in friendship it is a component of every individual s sexual life It is considered noteworthy or pathological when it exists in the place of heterosexual interests and love and when it becomes the only obligatory compulsive avenue of sexual expression

Incest —Incest is a sexual relationship between close blood relations (brother and sister parent and child) The discovery of the presence of unconscious incestuous desires in all humans is one of the most important results of psychoanalytic research Incest between siblings is far from rare in childhood and adolescence

Nymphomania —Nymphomania a *compulsion neurosis* focussed on genital activity consists of an excessive insatiable impulse in women to heterosexuality

Perversions —Perversions are sexual practices which markedly deviate from the so called normal or average Previously the subject of perversions vastly preoccupied psychiatrists but as psychoanalytic research has widened knowledge of sexual behavior the use of the term is more restricted and the concept less emphasized Many practices formerly looked on as perverse are now understood to be concomitants of normal sexual intercourse especially the milder variants employed in sexual foreplay Perverse tendencies become perverse only when they compulsively dominate sexual behavior to the exclusion of normal activity

Satyriasis —Satyriasis the male equivalent of nymphomania is excessive insatiable heterosexual needs Although the excessive activity occurs in the sexual sphere the drive which actuates the satyrism need not necessarily be erotic despite its cloak

Voyeurism —Voyeurism or peeping is sexual pleasure obtained by looking at the genitals or genital activities of another The looking is itself the ultimate aim of the sexual act and the act is usually committed secretly

Masochism —Masochism is that condition in which sexual satisfaction depends on the subject himself 'suffering pain ill treatment and humiliation" (Freud) It is characterized by the conscious or unconscious need to experience pain to achieve full sexual gratification

Sadism —Sadism is the accomplishment of sexual gratification from the infliction of pain on others It may vary from overtly perverse behavior as in whipping to the unconscious sadistic component of erotic practices as in humiliating or ill treating the love object A mild sadistic element is not infrequently present in normal love making as gentle biting

SEXUAL FUNCTION

Ejaculatio Praecox —Ejaculatio praecox is a condition in which ejaculation and detumescence occur before or too soon following entrance to permit satisfactory intercourse for man or woman It is a common *neurotic disturbance* of sexual function (p 2408)

Ejaculatio Retardata —Ejaculatio retardata is the relatively rare inability to achieve orgasm despite prolonged intercourse It may result in painful *intercourse with swelling and irritation of the penis* Mild degrees are not rare and often alternate with ejaculatio praecox

Frigidity —Frigidity is the inability of the female to achieve orgasm despite the genital adequacy of the male Although commonly used to refer to genital failure it also applies to absence of sexual feelings in general It may disappear and re appear under special circumstances

Impotence —Impotence is interference with the male capacity to have sexual intercourse the inability to have and maintain an erection It may be relative or absolute organic or psychogenic, it may vary with different women and under different circumstances A man may be potent with a prostitute and impotent with a woman for whom he has feelings of love he may be potent at the beginning of but lose his erection during intercourse The organic aspects of impotence are elsewhere described (p 2409)

Priapism —Priapism is persistent abnormal painful erection of the penis usually without accompanying conscious sexual desire The priapism may last from hours to weeks and lead to secondary changes in the corpora cavernosa It occurs in cord lesions and leukemia or it may be psychogenic In the latter instance a course of intensive psychotherapy is indicated along with the use of sedatives and relaxation baths Occasionally spinal or epidural anesthesia must be employed to obtain a brief respite

Spermatorrhea —Spermatorrhea refers to the spontaneous discharge of spermatic fluid usually without evidences of sexual desire or erection

Dyspareunia —Dyspareunia indicates painful intercourse and since it may be due to technical and organic as well as psychogenic causation it is elsewhere discussed (p 2491)

SLEEP

Normal sleep is characterized by the suspension of consciousness absence of reactivity to environment increase in the thresholds of general

DIFFERENTIAL DIAGNOSIS OF

Insomnia

Without knowledge of the causation of insomnia drug therapy holds little promise First principles in management consist of efforts to remove or correct etiologic factors

CAUSE	DIAGNOSTIC FEATURES
Errors in Hygiene	Excitement, anxiety fear fatigue overheated or chilled room, bad ventilation, undue noise or light, excessively soft or hard mattress too many or too few bedclothes too many pillows insufficient activity during day or undue amount of sleep and late nap in afternoon or evening
Pain	Especially with nocturnal exacerbations as in peptic ulcer and disturbances of bone
Fever	*Particularly in infections characterized* by night sweats such as tuberculosis and rheumatic fever Check fever chart, sputum get skin test and sedimentation rate
Drugs	Caffeine (coffee tea and cola drinks) Alcoholism Adrenergens (amphetamine ephedrine and allied preparations) Toxic doses of thyroid extract. *Idiosyncrasy to opiates*
Neuroses	Particularly in anxieties (pavor nocturnus) neurasthenia and hypochondriasis
Psychoses	Schizophrenia manic-depressive episodes and general paresis Examine spinal fluid (p 3734)
Neurogenic	Particularly cerebral arteriosclerosis and encephalopathies
Metabolic	In rickets hyperthyroidism, diabetes mellitus (polyuria) renal insufficiency (nocturia) and pruritic conditions Examine urine Obtain blood chemistry (p 3712) and B M. R. for therapeutic indications
Circulatory	With orthopnea due to backward failure (p 941) From *paroxysmal cardiac irregularities* (p 873) With night terrors especially in aortic disease and pericarditis (p 1007) Check physical findings with x ray and electrocardiogram.
Gastro-intestinal	Hunger pain in peptic ulcer Gastric dilatation due to retention or a meal at bed time *Constipation and distention. Fermentation and* diarrhea Nausea and vomiting Supplement examinations of stool and gastric contents with barium x rays
Respiratory	Nasal obstruction and post nasal drip Cough expectoration or dyspnea Check physical findings with x rays of sinuses and chest.
Genito-urinary	*Ungratified eroticism. Nocturnal emissions* Dysuria polyuria urinary retention and urinary frequency Examine urine and prostate
Pregnancy	From size of uterus or activity of fetus
Neuromuscular	Particularly with back pain and cramps in the thighs and calves

sensibility and reflex irritability, diminution of the basal metabolic rate lowering of blood pressure and a slight rise in temperature

The nature of sleep is still in dispute Pavlov believed that sleep was due to cortical inhibition There is accumulating evidence of the existence of a *sleep regulation center* in the mesencephalon the region in the peri ventricular gray matter of the third ventricle the neighborhood of the infundibulum or the mesial parts of the thalami In man, nocturnal sleep is regarded as normal The criterion of a satisfactory period of sleep is a feeling of rest and refreshment after awakening

Many of the popular legends about sleep have little basis in physiologic fact The ritual of the need for one long period of sleep in twenty four hours and of the necessity for remaining asleep a certain number of hours is a matter of custom more than anything else Animals sleep at frequent short periods throughout the day, a short nap may provide considerable rest and refreshment whereas a prolonged sleep may be followed by a sense of fatigue and heaviness

Insomnia —Insomnia occurs in three forms There may be inability to fall asleep but a sound sleep once sleep is achieved, there may be a tendency to waken repeatedly as the result of terror dreams throughout the night there may be no difficulty in falling asleep but early wakening with in ability to return to sleep Each variety of insomnia requires different man agement the patient who has difficulty falling asleep should have a rap idly acting soluble drug whereas those who waken repeatedly or in the early hours of the morning do better with the insoluble barbiturates (p 3839)

Treatment of Insomnia —Insomnia is best managed by elimination of the cause The use of drugs is postponed until other measures have been exhausted

1 Correct errors in hygiene particularly relative to the bedroom
2 *Discontinue naps during day or early evening*
3 Walk before retiring or at least exercise before open window
4 Omit fluids after dinner in those with polyuria nocturia or fre quency
5 Omit feedings after dinner in those who suffer gastric retention or flatulence
6 Give feedings of milk and crackers or soup for those with hyper motility or peptic ulcer
7 Evacuate rectum with suppository or rectal flush in those who com plain of flatulence
8 Stop all stimulant drugs
9 Forbid coffee tea and cola drinks after 4 P.M
10 Reduce alcohol to total two daily drinks Suggest hot toddy at bed time
11 Advise warm tub or bed sponge before retiring for febrile with nocturnal sweats
12 Arrange pillows for orthopneic cardiacs
13 Suggest steaming at bed time for respiratory sufferers with post nasal drip or cough Avoid sprays and drops with adrenergens
14 Finally if necessary prescribe soluble hypnotic such as *seconal so*

dium 100 mg (1½ grains) for rapid action, *sodium amytal* 180 mg (3 grains) for delayed action, and *tuinal* (equal parts of seconal and amytal) 180 mg (3 grains) for combined effects

Inversion of Sleep Ratio.—Inversion of sleep ratio is a condition in which the patient sleeps by day and has insomnia at night. The nocturnal insomnia may be associated with aggressive sexual behavior and voracious eating. It is found in maladjusted young people, *chronic encephalitis* and *schizophrenia*.

Narcolepsy.—Narcolepsy is characterized by short spells of uncontrollable sleep lasting from minutes to hours. It occurs under circumstances ordinarily associated with wakefulness, as for instance at work. At times the patient is not really asleep but is in a sort of trance; he is usually fairly alert when attentiveness is demanded but slips easily into sleep. During the narcoleptic spell the patient is relaxed, his color is good, the pulse rate is slow and breathing is slow and regular. The condition may be set off by sudden emotion, either pleasurable or unpleasurable. The patient, once asleep, is easily aroused. Nocturnal sleep is usually normal.

The pathology and etiology of this condition are not known, but it is observed in *subacute encephalitis*, following *head trauma*, in *cerebral neoplasms*, especially those of the third ventricle, and associated with *epilepsy*. It is believed that the attacks are due to involvement of the mesencephalic centers or inhibition of various parts of the central nervous system.

Somnolence.—Somnolence is unnatural sleepiness or drowsiness, usually at inappropriate times, such as at work, in the theater or in the classroom. It may be related to *hypothyroidism*, but most commonly is seen in the *neuroses*.

Treatment of Somnolence and Drowsiness.—The management of somnolence involves correction of hygiene and the use of metabolic and pharmacologic measures.

1. Eliminate errors in hygiene
2. Treat nocturnal insomnia (p 1706)
3. Prescribe low calory diet for obese (p [illegible])
4. Proscribe alcohol
5. Stop use of sedatives
6. Give thyroid extract in conditions of hypometabolism (p 1180)
7. Give androgen or estrogen in climacteric states (p [illegible])
8. Suggest morning purge with 1 or 2 teaspoonfuls of sodium bicarbonate and two glasses of hot water on arising
9. Provide for clearing of airway with steaming or nasal sprays
10. Order hematinics (p 1018) in anemias
11. Finally, prescribe amphetamine sulfate 2.5 to 10 mg on arising with repetition at noon if necessary

Prolonged Sleep.—Prolonged sleep, as the name implies, is the simple prolongation of sleep from days to months. It is found most commonly in acute and chronic *encephalitis*.

Terror Dreams.—Terror dreams are those in which the anxiety attached

sensibility and reflex irritability, diminution of the basal metabolic rate lowering of blood pressure and a slight rise in temperature

The nature of sleep is still in dispute Pavlov believed that sleep was due to cortical inhibition There is accumulating evidence of the existence of a *sleep regulation center* in the mesencephalon the region in the periventricular gray matter of the third ventricle the neighborhood of the infundibulum or the mesial parts of the thalami In man nocturnal sleep is regarded as normal The criterion of a satisfactory period of sleep is a feeling of rest and refreshment after awakening

Many of the popular legends about sleep have little basis in physiologic fact The ritual of the need for one long period of sleep in twenty four hours and of the necessity for remaining asleep a certain number of hours is a matter of custom more than anything else Animals sleep at frequent short periods throughout the day, a short nap may provide considerable rest and refreshment whereas a prolonged sleep may be followed by a sense of fatigue and heaviness

Insomnia —Insomnia occurs in three forms There may be inability to fall asleep but a sound sleep once sleep is achieved there may be a tendency to waken repeatedly as the result of terror dreams throughout the night, there may be no difficulty in falling asleep but early wakening with inability to return to sleep Each variety of insomnia requires different management the patient who has difficulty falling asleep should have a rapidly acting soluble drug whereas those who waken repeatedly or in the early hours of the morning do better with the insoluble barbiturates (p 3839)

Treatment of Insomnia —Insomnia is best managed by elimination of the cause The use of drugs is postponed until other measures have been exhausted

1 Correct errors in hygiene particularly relative to the bedroom
2 Discontinue naps during day or early evening
3 Walk before retiring or at least exercise before open window
4 Omit fluids after dinner in those with polyuria nocturia or frequency
5 Omit feedings after dinner in those who suffer gastric retention or flatulence
6 Give feedings of milk and crackers or soup for those with hypermotility or peptic ulcer
7 Evacuate rectum with suppository or rectal flush in those who complain of flatulence
8 Stop all stimulant drugs
9 Forbid coffee tea and cola drinks after 4 P M
10 Reduce alcohol to total two daily drinks Suggest hot toddy at bedtime
11 Advise warm tub or bed sponge before retiring for febrile with nocturnal sweats
12 Arrange pillows for orthopneic cardiacs
13 Suggest steaming at bed time for respiratory sufferers with post nasal drip or cough Avoid sprays and drops with adrenergens
14 Finally if necessary prescribe soluble hypnotic such as *seconal so*

ality structure The material that has detached itself from conscious control to form a secondary personality leads the individual from the ordinary places and activities of life Thus the patient may undertake a journey and find himself in a distant city with no conscious knowledge of why he made the trip how he arranged it or any of the details

Somnambulism —Somnambulism or sleep walking is the equivalent of the fugue except that it occurs during sleep In these acts either literally or symbolically the patient attempts to act out a desire or need which he cannot permit himself while conscious

The somnambulistic act and the accompanying dreams are not usually remembered The patient unless awakened returns to bed and resumes usual sleep Occasionally the somnambulist meets with an accident and suffers injury from a fall or from broken glass

Compulsion (Compulsive Act) —Compulsive or imperative acts are morbid irresistible urges to perform apparently useless and meaningless rituals They may be simple or complex They may afford unconscious gratification or protection to the patient or they may represent a substitute expression for the gratification of a repressed desire or experience

Repetitive Acts —Repetitive acts are forms of compulsive behavior in which the patient repeats simple acts such as counting the books on a shelf or the boards in the floor They may become complicated and burdensome as in many compulsive ceremonials The necessity of avoiding or renouncing these rituals may be accompanied by great discomfort and anxiety They are part of the syndrome of the *compulsion neuroses* (p 134˷)

Echolalia and Echopraxia —*Echolalia* is the meaningless repetition of words or phrases spoken by others It is an expression of automatic obedience Instead of answering a question for instance the patient repeats it again and again *Echopraxia* is the meaningless repetitive imitation of acts or movements performed by others in the patient s environment These phenomena are found in *schizophrenia*

Mania —Mania is a state characterized by exaggeration of ideas feelings and motor activity See *Manic Depressive Psychosis* (p 1368)

Hypomania —Hypomania is a less intense form of mania

Hypermania —Hypermania is a more intense form of delirious mania

Mannerisms —Mannerisms are gestures or other forms of expression characteristic of an individual In psychiatric patients mannerisms may become disproportionately important and acquire the significance of symptoms

Negativism —Negativism is opposite (negative) behavior or speech The patient characteristically does or says the opposite of what he is asked or expected to do This type of behavior is seen in *schizophrenia*

Paralalia (Speech) —Paralalia usually refers to any speech defect but may indicate the speech defect characterized by the substitution of one letter for another

Psychomotor Activity —Psychomotor activity is movement that is psychically determined the action resulting from an idea or perception It may be exaggerated (overactivity) diminished (underactivity) or disjointed (disactivity)

Stereotypy —Stereotypy is the constant seemingly meaningless repe-

to the content of the dream is so intense as to awaken the patient with tachycardia sweating restlessness and breathlessness

Hypnotic Sleep —Sleep induced through hypnosis is usually for diagnostic purpose, although occasionally the induced sleep itself is used directly *as a healing factor*

DIFFERENTIAL DIAGNOSIS OF

Somnolence and Drowsiness

The problems of somnolence are similar to those of insomnia with which they may be associated Rational therapy depends on the elucidation of the causative mechanism

CAUSE	DIAGNOSTIC FEATURES
Errors in Hygiene	From overheated room or insomnia of previous night From gluttony and over indulgence in alcoholic beverages With fatigue and excessive exposure to intense cold
Pharmacologic	Sedatives hypnotics and opiates
Neuroses	*Neurasthenia hypochondriasis* or *hysteria*
Psychoses	Schizophrenia depressed stages of manic depressive disorders and general paresis Examine blood and spinal fluid.
Neurogenic	In cerebral arteriosclerosis encephalopathies and encephalitides
Metabolic	Hypothyroidism acromegaly pituitary basophilism, Frohlich s *syndrome* adrenal cortical insufficiency hypogonadism diabetes mellitus and uremia *Get urinalysis (p 3667)* blood chemistry (p 3712) and B M R. for therapeutic indications
Gastro intestinal	With obstipation and auto-intoxication
Respiratory	With apro exia especially in upper respiratory infections
Blood Disorders	Especially with anemias Get hemogram (p 3704)
Infectious	In epidemic encephalitis and trypanosomiasis

MOTOR BEHAVIOR

Motor behavior is judged by the neuromuscular activities of the patient in his gait speech posture expression and activities

Abasia —*Abasia inability to walk is usually associated* with *astasia* inability to stand erect

Astasia abasia —Astasia abasia is a symptom of mental conflict most commonly found in *hysterical conditions* It consists of an inability to stand or walk and is based on abulia a loss or deficiency of will power

Automatism —*Automatism is a condition in which activity is carried* out without conscious knowledge It is seen in *catatonic schizophrenia* and in certain *hysterical states* Tics may be considered as automatisms

Fugue —The fugue or flight is an expression of dissociation in person

CHAPTER 61

PSYCHIATRY THE ETIOLOGY, CLASSIFICATION AND DIAGNOSIS OF MENTAL DISEASES

THE ETIOLOGY OF MENTAL DISEASE

THE mechanisms by which the nerve cells and tissues become deranged do not differ from those that are operative in the other organs of the body Cellular injury and death result from physical and chemical causes from trauma from the invasion of neoplastic tissue from the effects of infectious processes (particularly syphilis) from nutritive disorders arising from vascular disease and occlusion and from poisonings as the result of the influences of drugs or chemicals arising endogenously in the course of disturbed metabolic processes or of exogenous origin in occupation or criminal poisoning

Beyond these tangible and often demonstrable mechanisms there is a vast reservoir of mental disease in which neuroses and psychoses and disturbances in personality and character arise without demonstrable exogenous cause and in which there are no clearcut pathologic changes These states are obviously disorders of a functional nature often arising as the result of derangements in cerebration or the emotional development of the individual

Organic Disease —The histopathologic forms of mental disease include the *congenital abnormalities* such as mental deficiency the *infectious states* particularly syphilis the *traumatic and post traumatic afflictions* the *vascular group* secondary to arteriosclerosis the *psychoses associated with neoplastic disease* and *miscellaneous neurologic disorders* such as multiple sclerosis and paralysis agitans Afflictions in these categories are essentially secondary manifestations of more fundamental tissue derangements and management is directed toward the correction or elimination of the noxious origin See p 1374

Toxic or Metabolic Derangements.—Mental diseases due to toxic or metabolic derangements are rarely associated with demonstrable histologic change but the offending substance may often be suspected or demon

tition of any act The maintenance over long periods of a fixed posture or place has also been called stereotypy It is seen in *schizophrenia*

Tics —Tics are involuntary movements of certain muscle groups The resultant motion resembles an organized action in contrast to other in voluntary motions Tics may be organically induced or psychogenic the latter sometimes being spoken of as habit tics

Verbigeration —Verbigeration is the meaningless repetition of sentences phrases or words It is stereotypy as expressed in language and is encoun tered in *schizophrenia*

SPEECH

The accomplishment of speech is an attribute almost wholly limited to human beings It is a highly complex neuromuscular activity

Aphonia —Aphonia indicates loss of phonation although articulation is preserved The patient talks in a whisper It is most commonly found in *hysteria* but it may be due to bilateral paralysis of the vocal cords or disease of the larynx (*q v*)

Mutism —Mutism is the state of being dumb silent or voiceless in the absence of structural changes (deaf mutism) It results from psychic causes and is commonly associated with negativism It represents a re fusal to talk and is seen in *schizophrenia depressions involutional melan cholia* and *hysteria*

Stuttering Stammering —Although some specialists in the disorders of speech distinguish between stammering and stuttering in general usage the latter is considered a more violent form of the former Each is char acterized by spasmodic utterances and blocking breaks and repetitions usually associated with sputtering The difficulty may be constant or ap pear only under emotional stress Occasionally stutterers can sing without noticeable difficulty

There is some suggestion that stuttering is organic and that it results from emotional factors exerting their influences on a definite nucleus Often it is hereditary and may be related to handedness or dominance

POSTURE

Cataplexy —Cataplexy consists of paroxysmal attacks induced by emo tional excitement such as intense laughter or irritation in which there is postural collapse of the whole body with loss of muscle tone The per son sinks to the ground consciousness may or may not be lost but the deep reflexes are abolished Cataplexy is usually grouped with *narcolepsy* as a variant of the paroxysmal disorders The cause is not *definitely* known

Cereaflexibility —Cereaflexibility is the wax like flexibility and immo bility of the extremities met in catatonic stupors The extremities placed in any awkward uncomfortable position are maintained for abnormally long periods of time

Catalepsy —Catalepsy is usually used synonymously with flexibilitas cerea It may refer to any form of sustained immobility These states are most common in *schizophrenia* and *hysteria*

This apologetic introduction is planned to placate erudite specialists who may be assured that every effort has been made to avoid the perpetration of excessive violence to current psychological and psychiatric concepts It is the present plan to subdivide mental disease into (1) those conditions characterized by *mental deficiency* which are measurable through intelligence quotients the less tangible but by no means less real (2) *neuroses* (3) *idiopathic psychoses* and (4) *symptomatic psychoses*

Mental Deficiency —The conditions of idiocy imbecility and moronity are discussed in Chapter 63 (p 1332)

Definition of Neurosis —The neurosis is a psychological disturbance that arises as a reaction to stress It is unaccompanied by any serious alterations in the evaluation of reality It is a *partial reaction* in that the personality is otherwise well integrated and socially organized It is more common and usually less severe and disabling than the psychosis

Definition of Psychosis —The psychosis is a total personality reaction that is disabling and severe The personality is distorted and disorganized and the appreciation of social and sensory reality is entirely destroyed

TABLE 86 —FACTORS DIFFERENTIATING NEUROSIS FROM PSYCHOSIS

Neurosis	Psychosis
Partial reaction	Total reaction
Less severe	Disabling and more severe
Anxiety and compulsion behavior of thoughts	Hallucination and delusion
Personality remains socially organized	Personality distorted and disorganized
Appreciation of social and sensory reality seriously affected	Appreciation of social and sensory reality entirely destroyed
No great interference with reality testing grasp of social relationship and appreciation of external world not seriously compromised	Grasp of social relationship and appreciation of external world greatly compromised

and often replaced by hallucination and delusion The grasp of social relationships and the appreciation of the external world situation are greatly compromised and the afflicted patient is greatly incapacitated in so far as normal interrelationships are concerned

Distinction Between Neurosis and Psychosis —The differential diagnosis between the neurosis and the psychosis is of utmost importance in the arrangement of a therapeutic program and in prognosis It is summarized in Table 86

Idiopathic Psychoses —The idiopathic psychoses are those in which there is no demonstrable etiologic agent The most important of these baffling and disturbing clinical entities are schizophrenia (p 1364) and manic depressive insanity (p 1368)

Symptomatic Psychoses —The symptomatic psychoses are those in which the mental aberration complicates a more fundamental anatomic or functional disturbance The commoner etiologic factors are trauma fever infection neoplasm cerebral vascular disease metabolic derangements poisonings and neurogenic disorders

strated *Endogenous* metabolic causes include fever acidosis azotemia, hypoglycemia hyperglycemia avitaminosis and endocrinopathies *Exogenous* toxic agents which produce mental disease, include alcoholism saturation of the nervous system with metals particularly lead mercury and arsenic, and the chronic use of opium derivatives bromides cocaine and barbiturates See p 3839

Functional Disturbances—The mental disorders that arise without tangible histopathologic chemical or metabolic causation are more difficult of definition classification and treatment Since these afflictions particularly the neuroses constitute the vast reservoir of mental disease seen in clinical practice they offer a real challenge to the practitioner who is required to have some concept of their nature if he is successfully to deal with them

Dynamic Psychology—Students of dynamic psychology explain functional mental afflictions in terms of the *conflicts* which inevitably result from the inability of the individual to adjust himself to his environment and his society In our civilization each of us is subject to disappointment frustration stress and anxiety There is necessarily some measure of emotional conflict which must influence and sometimes cause mental illness Our present civilization allows for many of us highly inadequate expressions of our needs We are compelled to curb desires school ourselves in disappointment and wait upon the achievement of ambitions We must regulate our behavior repress our emotions and wishes and fit our individual expressions to the environment and society in which we live The necessary compromises may be reflected by the production of neurotic behavior psychosomatic disturbances or actual psychoses

Freudianism—The monumental contribution of Sigmund Freud seems best adapted to function as a working hypothesis for the clearer understanding and more intelligent management of the common neuroses as seen in private practice This statement is not to be interpreted as a wholehearted and complete acceptance of all the theories of Freud, nor is it to be regarded as indicating that the practitioner should become a psychoanalyst or necessarily refer his patients to the accredited specialists for psychoanalytical therapy It is sufficient in this place to emphasize that the acceptance of the Freudian theory of the neuroses and the approval of widespread psychoanalytic therapy constitute separate and distinct discussions Freud himself has made this clear when he wrote the future will probably attribute far greater importance to psychoanalysis as the science of the unconscious than as a therapeutic procedure

THE CLASSIFICATION OF NERVOUS AND MENTAL DISORDERS

The exigencies of the general practice of medicine require that the practitioner who is concerned with all of the branches of his profession be provided with expositions of specialist fields expressed in terms sufficiently plain so that they are readily comprehended and yet not so simplified as to rob the material of its meaning With these requirements in view and with due reverence and apologies to neurological specialists and psychiatrists the following classification is tentatively presented for present usage It is intended to furnish the practitioner with an intelligent concept of mental conditions and a definitive method of managing the afflicted patient

dwells on friendships religious attitudes and concepts social and community responsibilities and reactions to authority On a more personal basis the patient is questioned as to emotional fluctuations reactions to disappointment and success attitudes toward money conscientiousness punctuality hypersensitivity irritability mood changes personal habits and the presence of phobias or compulsions

When it comes to a discussion of the present illness the patient is requested to express an opinion as to causative mechanisms situations or occurrences This viewpoint may be supplemented or corroborated by a mother father wife husband child or other member of the family preferably quizzed in the absence of the patient The acquisition of these data does not require any particular training or special aptitude though it is time consuming The whole history often cannot be obtained in one formal sitting but may be pieced together over a period of time after a number of contacts

Physical Examination—The physical examination of the psychiatric patient must be most exhaustive In addition to the routine survey a gross neurological examination is mandatory the fundus oculi must be scrutinized and a temperature record must be recorded See also p 3468

Laboratory Data—The history and physical examinations in psychiatry require supplementation by a battery of laboratory tests including routine urinalysis hemogram (p 3704) blood chemistry basal metabolic rate determination and a serologic test for syphilis (p 337) In the presence of severe or persistent disorders cerebrospinal fluid is obtained evidences of increased intracranial pressure are sought and the fluid is examined for its cytologic bacteriologic and serologic characteristics and for colloidal gold reactions (p 3737)

Neuropsychiatric Consultation—The neuropsychiatric consultant is utilized freely by the sage practitioner In highly specialized institutions reference is made to psychiatrist organic neurologist and neurosurgeon Additional examinations include radiography of the skull electroencephalography ventriculography encephalography and laminography Psychometric tests may be required (p 1395) An ophthalmologist may be called for more accurate delineation of the changes in the visual fields or the fundus oculi (p 1545) The otologist is asked to perform audiometry and vestibular tests (p 2017) In desperation it may be necessary to perform an exploratory craniotomy or laminectomy In the end the practitioner often finds himself beyond his depth in his attempt to integrate specialist findings and under these circumstances it is wise to call in a seasoned internist to act as referee (p 3899)

THE DIAGNOSIS OF MENTAL DISFASE

The diagnosis of mental disease places a severe tax and responsibility upon the practitioner After the recognition of the psychiatric component it becomes necessary to define the diagnosis in terms of mental deficiency neurosis, idiopathic psychosis or symptomatic psychosis and then seek to determine or exclude the presence of local or systemic disturbances of more fundamental etiologic significance

The practitioner owes it to the patient and himself to arrive at the diagnosis of the neurosis or the idiopathic psychosis only through the tedious methodology of exclusion Once having conducted his survey he must pave the way for re investigation at stated intervals since latent processes may reach the surface of clinical recognition after periods of months or years Exemplifying this are examples of brain tumor with herald psychiatric manifestations and later organic findings definitely not present at the initiation of the difficulty

History —The psychiatric history must be broad in scope since the sub ject matter deals with all processes which disturb the adjustment of the patient compromise his attainment of ordinary gratification deprive him of a proportionate amount of happiness and self satisfaction and limit his capacity to get along with his fellows within the social structure of the community in which he dwells The psychiatric history concerns itself with the individual in the broadest aspects of his bodily health It deals with his social marital and business adjustments moods and reactions to the problems of every day life

The psychiatric examination need not be conducted on a formal basis The patient is put at his ease and given every opportunity to dilate on his individual problems In the course of the discussion inquiry is made concerning the incidence of nervous and mental disorders alcoholism syphilis and epilepsy in the family If it is possible a birth history is ob tained particularly with reference to length of labor use of instruments and the amount and degree of asphyxia Emphasis is placed on childhood development particularly such factors as weaning cleanline s temper tan trums masturbation and thumb sucking Some idea should be obtained of early family training with particular reference to the position of the pa tient in the family circle and in relationship to grandparents parents brothers sisters and household servants Early personality traits are im portant, especially in contacts with other children The school history deals with scholastic progress disciplinary problems crushes' on school mates and teachers participation in sports and extracurricular activities and rela tive academic standing It is necessary to establish thorough information concerning psychosexual adjustments The patient is quizzed concerning masturbation homosexual manifestations whether overt or implied hetero sexual adjustment premarital marital and extramarital intercourse atti tudes toward the conjugal partner and children and deviations in sexual practices

Equally important are the histories of work and social adjustments The patient s attitude to business profession or household is noted Em ployees are questioned concerning their ability to stick to a job and take orders Employers are interrogated concerning ambitions attitudes to em ployees and competitors and their feelings of security The social history

ple mechanism of an outpouring of hatred injustice or intolerance fancied or real

There is no contraindication to the practitioner functioning as a passive psychotherapist In exchange for the time expended his patient for whom he has actually performed no active service may leave his presence assured and assuaged

Information Interpretation and Explanation—Much of the usefulness of the practitioner is related to his role as a pedagogue dealing with the problems of general hygiene Many fears are based on erroneous conceptions of physiologic facts The teachings of body hygiene dietotherapy intestinal and sexual habits and the care and feeding of children and their parents are part of the routine of private practice Expositions of these problems should be given simply and without condescension or under estimation of the nature and extent of the anxiety which misconceptions may engender The discourse should be in the vernacular avoiding technical terms which serve to confuse the auditor

As a corollary to the dissemination of information the practitioner functions *to correct misinformation* All that many patients need to be told is that old wives tales are just not so For example it is not necessary to have a bowel movement each day frightening the pregnant woman does not produce congenital malformation of the child masturbation does not result in rings under the eyes or acne vulgaris eating meat does not cause elevation of blood pressure nor the combination of bananas and water a fatal indigestion a blow on the female breast does not produce cancer any more than eating acid foods produces rheumatism venereal disease is not acquired on a toilet seat nor is pregnancy the result of bathing in a tub previously used by a younger brother The anxieties that arise from these myths can often be dissipated by statements of simple fact Persistence of the symptom despite lucid explanation serves as a *therapeutic test* and indicates that the disturbance is on a more profound level The rigidity of the neurosis then is such as to require specialist care

Reassurance—In a positive way psychotherapy is best practiced effectively when the physician gives his patient reassurance Most patients consult their physician with an *aura of anxiety* If a finger is cut there is dread of infection the presence of a lump precipitates cancerophobia and an excoriation of the penis brings fear of syphilis Frequently the patient comes to relieve his anxiety rather than to submit to therapy Reassurance that his fears are unwarranted is accordingly a powerful psychotherapeutic measure

Complete physical examination is perhaps the most potent method of providing reassurance but excessive examination with a formidable battery of tests may lead the anxious patient to assume the presence of serious illness During his investigation the practitioner must not indulge in careless or technical conversation lest the patient develop a sense of insecurity from the use of words foreign to his everyday conversation To the anxious patient a lump means cancer a murmur heart trouble absent reflexes imminent insanity infected tonsils septic poisoning

Lending Moral Support—In emergencies the physician s very presence supplies moral support which may be more beneficial than medication

CHAPTER 62

PSYCHOTHERAPY

NON-TECHNICAL PSYCHOTHERAPY

For the most part except in expert hands psychotherapy is a guile less and unobtrusive exercise The practitioner indulges in it when he smiles reassuringly upon entering a sick room when he pats his patient s hand or spends the night in the home of a desperately sick patient friend hopelessly afflicted with an inoperable carcinoma when he discounts 50 to 100 mm of mercury in giving a blood pressure reading to an anxious and unstable individual, and when he prescribes a placebo for his patient and surrounds the prescription with the trappings of a potent drug Each prescription that is written each injection that is given and each proce dure that is executed is clothed with an aura of hope trust and faith This may not be the intent of the physician at all times but it is implica tion received by the patient

Notwithstanding their protestations to the contrary the technical spe cialists including the surgeons practice psychotherapy The operator is a psychotherapist when he reassures us who are on the cutting end of the scalpel that it won't hurt and when he asserts that the intended proce dure is without discomfort morbidity or mortality ' For the most part massage and physiotherapy particularly with electrical apparatus owe their beneficences to the element of suggestion

Few therapeutic modalities are more important and more potent than psychotherapy None requires such tender devotion or respect for once lost faith like virginity can never be regained

THE PRACTITIONER AS A PSYCHOTHERAPIST

The practitioner psychotherapist may serve his patient in good stead *without great formal training Equipped only with patience* good com mon sense and a sympathetic desire to be helpful he is capable of han dling all but the most difficult challenges

Ventilation —At times the practitioner needs only to listen sympathet ically to the recital of his patient's problems and tribulations The major ity of disturbed individuals ask for no more than an attentive ear and some intangible evidence of understanding listening Ventilation is as an cient as the religious confessional and as new as the *catharsis* of certain forms of modern analytic therapy It is a form of therapy that has great power for good and little prospect for evil It relieves tension by the sim

The practitioner should give as little advice as possible and aim to guide the patient in the working out of a solution for his individual problem It is good discipline to suggest to the patient after the facts have been gathered to sleep on the matter and then make an attempt to think things out This serves to stimulate initiative and from the practitioner s point of view terminates a protracted interview

The giving of advice has at least one other advantage in that the patient may find himself incapable of executing the suggestion however sound and appropriate As a result he develops even greater feelings of insecurity and doubt defeating the intended therapeutic purpose and erecting a barrier between advisor and advised

Play Hobbies and Recreations—The physician should have an accurate knowledge of the occupational and diversional facilities that are available in his community The cultivation of hobbies indulgence in educational and artistic opportunities exercises or sports and an acquaintance with nearby places of sanctuary and refuge constitute psychotherapeutic devices of considerable importance The ingenious physician often succeeds well in utilizing even the meager resources of his locale

Rest and Relaxation—There is no possible manner of overestimating the beneficences of rest and relaxation At times the physician accomplishes this for his patient by suggesting the interpolation of a rest period or nap after luncheon in the middle of the day or after the evening meal A housewife may be relieved of some of her household duties by requesting more cooperation and thoughtfulness from her children Reference is made elsewhere (p 3755) to the devices of the partial rest cure consisting in spending part of the day in bed or loafing for a weekend (p 3754) More elaborate devices include the complete rest cure (p 3754) using the Weir Mitchell technic (p 3754) or a modification thereof Wealthier patients gild their infirmities by taking a vacation or visiting a spa (p 3764) preferably one at a great distance

Occupational Therapy—The use of occupational therapy in the home requires only the exercise of ingenuity by patient or physician Reference is made elsewhere (p 3764) to the amazing frequency with which the most unlikely candidates are found to show interest and talent in the exercise of the arts in labor industry or for the sheer enjoyment of accomplishment Manual laborers often show a surprising ability in creative art and sedentary or intellectual workers exhibit considerable manual dexterity at their hobbies

Study Programs Bibliotherapy and Reeducation.—Just as occupational therapy provides a preoccupation with manual accomplishment so the mind of the patient is often stimulated and directed into more proper channels by study programs reeducation and reading These devices are of particular importance in the management of the maladjusted adolescent If the physician has got out of touch with the available reading material he may call upon local members of the teaching profession or the librarian in the neighborhood to assist in arranging a reading list

Religion and Philosophy—Older patients and particularly those who are nearly at the end of their earthly existence often strive for a star to which they may hitch their wagon The safest and best expedient is organized religion If the local clergyman exhibits an interest in problems

Human beings are frequently buffeted by dire and tragic events beyond medical assistance These may be endured with fortitude through the support and understanding of the physician friend The patient ill with pneumonia derives more comfort from the knowledge that his doctor is sleeping in the house or sitting at the bedside than from many of the 'stimulants of the pharmacopeia The physician must not underrate or be heedless of, the therapeutic effect of his presence alone even though he may be embarrassed by his impotence with the more tangible therapeutic modalities Sympathy in the practice of medicine is like the air on the inside of a tire There may be nothing to it but it eases many a jolt and saves many sore spots" (*Neighbors*)

Persuasion and Suggestion—Persuasion and suggestion are powerful psychotherapeutic modalities Most of the 'faith healers employ these agencies with deliberation and cunning

It is morally wrong for the practitioner to exploit the patient who has been given an abiding faith but there is nothing culpable in the use of persuasion and suggestion when these measures are indicated The practitioner may for example urge greater understanding between parent and child or child and parent he may attempt to get a toper on the water wagon he frequently has to urge an errant marital partner to return to his home He attempts to cajole the obese into dieting the chain smoker into the temperate use of tobacco the overconscientious worker or housewife into seeking a vacation or relaxation and the sluggard to assume the responsibilities of everyday life

Persuasion largely uses intellectual forces to oppose the emotional factors involved in the production of conflicts and symptoms Unfortunately the intellect is frequently a puny instrument with which to regulate behavior and feeling The experienced learn not to expect a great deal from appeals to intelligence logic or a sense of decency *Suggestion* is helpful in many anxiety conditions Often the timorous and insecure require a symbol to guide their decisions strengthen them in their purposes and sustain them in hours of evil This symbol may be an intangible vote of confidence from the doctor a placebo or a vitamin pill

Advice—A hazardous but alluring form of psychotherapy is the giving of advice This two edged psychotherapeutic agency appears to be simple and confers a great sense of power on the advisor who usually projects his own whims or attitudes in a given situation The physician who is a total abstainer entertains a different attitude toward alcohol from his colleague who enjoys a cocktail or highball with his evening meal The golfing yachting or gardening enthusiast sees his hobby as a solution for all problems The happily married benedict swears by matrimony but the physician with a nagging wife and ubiquitous mother in law advocates divorce or single blessedness If advice is to be given the physician should attempt an objective attitude shelving for the time being his own likes and dislikes

Advice must be within the patient s potential capacities A day laborer cannot of course take up golf and the city dweller cannot do gardening A housewife cannot take the day off if there is no one at home to prepare the evening meal and make the beds nor can her wage-slave husband take a weekend off or go sailing before it gets dark

The practitioner should give as little advice as possible and aim to guide the patient in the working out of a solution for his individual problem It is good discipline to suggest to the patient after the facts have been gathered to sleep on the matter and then make an attempt to think things out This serves to stimulate initiative and from the practitioner s point of view terminates a protracted interview

The giving of advice has at least one other advantage in that the patient may find himself incapable of executing the suggestion however sound and appropriate As a result he develops even greater feelings of insecurity and doubt defeating the intended therapeutic purpose and erecting a barrier between advisor and advised

Play Hobbies and Recreations —The physician should have an accurate knowledge of the occupational and diversional facilities that are available in his community The cultivation of hobbies indulgence in educational and artistic opportunities exercises or sports and an acquaintance with nearby places of sanctuary and refuge constitute psychotherapeutic devices of considerable importance The ingenious physician often succeeds well in utilizing even the meager resources of his locale

Rest and Relaxation —There is no possible manner of overestimating the beneficences of rest and relaxation At times the physician accomplishes this for his patient by suggesting the interpolation of a rest period or nap after luncheon in the middle of the day or after the evening meal A housewife may be relieved of some of her household duties by requesting more cooperation and thoughtfulness from her children Reference is made elsewhere (p 3755) to the devices of the partial rest cure consisting in spending part of the day in bed or loafing for a weekend (p 3754) More elaborate devices include the complete rest cure (p 3754) using the Weir Mitchell technic (p 3754) or a modification thereof Wealthier patients gild their infirmities by taking a vacation or visiting a spa *(p 3764) preferably one at a great distance*

Occupational Therapy —The use of occupational therapy in the home requires only the exercise of ingenuity by patient or physician Reference is made elsewhere (p 3764) to the amazing frequency with which the most unlikely candidates are found to show interest and talent in the exercise of the arts in labor industry or for the sheer enjoyment of accomplishment Manual laborers often show a surprising ability in creative art and sedentary or intellectual workers exhibit considerable manual dexterity at their hobbies

Study Programs Bibliotherapy and Reeducation —Just as occupational therapy provides a preoccupation with manual accomplishment so the mind of the patient is often stimulated and directed into more proper channels by study programs reeducation and reading These devices are of particular importance in the management of the maladjusted adolescent If the physician has got out of touch with the available reading material he may call upon local members of the teaching profession or the librarian in the neighborhood to assist in arranging a reading list

Religion and Philosophy —Older patients and particularly those who are nearly at the end of their earthly existence often strive for a star to which they may hitch their wagon The safest and best expedient is organized religion If the local clergyman exhibits an interest in problems

that bridge the narrow gap between medicine and theology he may prove of immeasurable assistance in the management of those who stand in the shadow of death Not only does he comfort the afflicted but his good offices relieve the practitioner of a heavy and exhausting burden It is a wise practice for the physician irrespective of his church affiliation or lack of one to *cultivate the local clergymen of all denominations so that* he and his patient may count on their cooperation in the resolution of com mon problems

The unbelievers and those not of formal religious denomination are often comforted by an introduction to the writings of the great philos ophers

Remotivation Sublimation and Substitution—Among the well to do pa tients in any practice there is a vast amount of difficulty that arises as the result of idleness and the pursuit of false gods Few successful men and women and fewer who inherit wealth are able to tolerate good for tune Easy money and leisure invite multiple and recurrent fractures of the Ten Commandments School children and college students on their prolonged holidays tend to get into all manner of difficulties merely for want of something better to do Alcoholism the excessive use of nicotine sexual aberrations and all manner of mischief may be the result of bore dom and lack of something to do While the leisure class has more oppor tunity to cater to such weaknesses it has no monopoly on this commod ity Precisely the same conduct disorders and neuroses are observed in the underprivileged and middle classes Whereas the pampered sot ends up in a Turkish bath the impoverished one finds himself in the local cooler or at the business end of his wife s broomstick *Who will say* which is better and more effectual therapy?

The compleat practitioner often is enabled to accomplish great things by practical remotivation The indolent and indulged housewife may sub stitute good work in the local philanthropic organizations for her card games and gossip Impressionable youngsters of school or college age sublimate their restless energies when in place of excessive indulgence in athletics or dance contests they are given responsibilities by an ingenious parent or physician

Autopsychotherapy—The greatest and most successful therapist for each patient is the doctor whose face appears in the mirror The accom plishment of any other physician is apt to be transitory and shortlived The patient who can be influenced to exhibit firm self control and will power has surely combated many difficulties that can be influenced in no other way These truths are best illustrated in the treatment of alcohol ism excessive smoking and the obesity that results from hyperalimenta tion In the latter instance all the diet lists in the world are ineffectual in the face of self indulgence Contrariwise the accomplishment of weight reduction is a simple exercise in the management of the patient who can and will adhere to a simple regimen

The appeal to autopsychotherapy serves as a therapeutic test Failure of the method as in alcoholism suggests the presence of a profound neu rosis requiring technical assistance from the specialist consultant

Placebos—Many doubts seem to exist in the minds of practitioners relative to the ethics and advisability of employing placebos While such

methods have been attacked by dwellers in ivory towers they serve a beneficial role in the hands of the modern physician We are rather inclined to doubt the sincerity of any practitioner who asserts that he does not employ them consciously or subconsciously This defense of placebos and suggestion is not to be interpreted as a brief for their unjustifiable exploitation in the hands of the unscrupulous within and without the medical profession An untutored and anxious patient must often be given something tangible to take The hurried and harried practitioner often resorts to a placebo when he has not the time to listen to or deal with an anxiety situation

The placebo may be employed for some purpose other than what appears to be its intent The patient may faithfully inhale steam when Tincture of Benzoin is added to the kettle but think poorly of the same therapeutic measure without the odor He may conscientiously soak a limb in a saturated solution of epsom salts when the same procedure would be neglected in tap water A child will gargle with a solution containing aromatic oils but not with saline A patient will return to the physician s office for hypodermic injections but not for further conversations that deal with a difficult situation

The addition of suggestion to the placebo is not without danger When the physician intimates to his patient that the administration of a remedy should or will result in alleviation of the symptoms he gambles with the patient s faith and his own reputation The afflicted sufferer does not forget nor forgive the continuance of symptoms for which relief has been promised He may harbor an antagonism for the physician as an individual and for the practice of medicine in general Those with the greatest capacity for faith have the greatest capacity for cynicism

When it becomes necessary to use a placebo or suggestion the physician hopes that the expedient will prove to be temporary He strives to build a firm relationship with his patient so that he can deal forthrightly honestly and directly in his future therapeutic endeavors

Adjustment of Family and Business Difficulties—At times the emotionally disturbed patient suffers from the shortcomings or afflictions of those with whom he is in contact A husband may be driven to desperation by a neurotic wife who has all manner of compulsions and obsessions so that his life at home is unbearable particularly at the end of an exhausting day of work The woman whose husband has a profound sexual neurosis rendering him impotent may be restless and irritable and sleepless and unstable to the point where she seeks medical assistance She requires relief from symptoms that are referable to her lord and master while he because of the nature of his affliction shuns the physician and denies any difficulties

In the business world the anxiety and symptoms of exhaustion of an employee or partner may be traced to a compulsion neurosis on the part of the head of a business whose driving power is more than his normal integrated associates can endure In academic life pupils often get into serious difficulties as the result of a neurotic tendency of the teacher who strives to compensate for frustrations by beating down the ambitions of young hopefuls In their own lives physicians see these mechanisms at work in hospital politics where the neurosis of one successful chief of

service may cloud and disturb the lives of most if not all of his junior associates

In situations such as these the practitioner is faced with a grave difficulty Under ideal conditions he attacks the problem on two fronts He attempts to desensitize his patient so that he is able to endure that which cannot be cured In a compact community the samaritan physician may also attempt to deal with the difficulty at its source and gratuitously consult with the first cause ' More often than not despite good intentions he leads with his chin and is fortunate indeed if he escapes with minor cuts and bruises

The Use of Drugs—The use of drugs in psychiatry is of minor significance *Sedatives* and *hypnotics* are useful in the treatment of conditions characterized by nervousness restlessness and insomnia Often however this therapeutic endeavor proves a two edged sword since the patient with a neurosis or psychosis is prone to become dependent upon the drug requires increased dosage and develops addiction A more serious complication particularly in the management of epilepsy is the superimposition of *chronic bromide intoxication* with its train of psychotic manifestations often of graver significance than the fundamental disorder

Most of the so called *nerve stimulants* owe their reputation almost entirely to suggestion Manganese phosphates neurophosphates lecithin strychnine caffeine and the like accomplish nothing that is pharmacologically demonstrable and they may be harmful *Amphetamine sulfate* (*benzedrine*) has proven a real boon however when judiciously used as a cerebral stimulant and *thiamine chloride* is a powerful stimulant to afflicted peripheral nerves

Consultation—For the vast majority of patients the simple devices outlined above suffice for an adequate therapeutic result In a small number of cases a more penetrating and basic form of psychotherapy becomes essential Because of the stigma and opprobrium which still attaches to mental disease the family practitioner is often understandably reluctant to suggest psychiatric help Some patients and many families resent this advice but when the physician has thoroughly exploited his resources to no avail it is his duty to refer the patient to a competent psychiatrist for formal treatment (p 1324) Failure of nontechnical psychiatry exposes the depth and rigidity of the neurosis serves as a therapeutic test and indicates the necessity for formal consultation and treatment

DETERRENTS AND IMPEDIMENTS TO PSYCHOTHERAPY BY THE GENERAL PRACTITIONER

It is unfortunate that psychotherapy by the general practitioner occupies the top of the list in the enumeration of his services for which he reaps ingratitude The patient who is emotionally disturbed is most profligate of the time energies and resources of his doctor and usually manages to upset an entire office hour an evening of anticipated rest and relaxation a holiday or a vacation

It is characteristic of the mental patient that he shifts doctors for no reason other than to manifest his fundamental insecurity to get revenge for what he considers lack of sympathy on the part of the previous listener or out of plain orneriness Add to this the fact that neither the

patient nor his family regard nontechnical psychotherapy as a service of sufficient dignity to warrant the payment of a fee and there results a circumstance in which the practitioner makes a maximum investment of time energy and skill for a minimum fee and a plethora of abuse and ill will

It would be misleading to indicate however that this gloomy prospect is unrelieved Increasingly as the public has become educated the cured neurotics and those who have been helped with their emotional and psychogenic problems become the loyal constituents and supporters of their doctor With the passage of time the practitioner regards with great satisfaction the souls he has saved through a conversation a bit of timely advice or a word or gesture of encouragement and faith given at just the right time The little boy who lied and stole at school becomes distinguished for courage and daring the little girl whose sexual curiosity made her the community plaything blossoms forth as a devoted mother and wife the insecure stripling finds a new world under a microscope in the field of music or science and comes of age the wastrel discovers that fun ain t fun and diverts his excessive energies into purposeful and useful endeavor Behind these minor miracles is often the figure of the doctor who did the right thing and said the right words at the right time often without any regard for the formalities of psychiatry or current concepts of habits and morals

The family physician plays down and even apologizes for his psychotherapeutic endeavor He is intimidated at least in part by the evolution of involved complicated and exhaustive formal psychiatric technics and their mysterious terminologies

Physicians who have their own emotional difficulties are often prevented from adequate psychotherapy by unsurmountable resistances and prejudices Some persist in the concept that emotional sickness is blameworthy They seem unaware of the anguish and waste of an emotional illness and the difficulty of reaching the problems of the sufferer Such physicians are relieved when freed of the onus of taking care of the patient with a psychogenic disturbance If the burden must be assumed the neurotic tendencies of the practitioner often make him unsympathetic and impatient and he projects his own difficulties into the problems presented by the patient thus unwittingly causing considerable damage

The general practitioner also is handicapped in his role of psychotherapist by his intimacy with the patient and the family circle It is difficult to discuss an emotional problem concerning which a patient has a sense of guilt or inadequacy with a companion or neighbor with whom there must be social intercourse Conditions analogous to these lead the psychoanalyst to refuse to treat friends or relatives The patient speaks more freely to a stranger Yet in many instances the practitioner because of personal intimacy with the background and home life of his neighbor patient knows the entire problem without being told and is enabled to cut corners and drive directly to the heart of the difficulty Much of success or failure in dealing with ethico social difficulties depends upon the attitude of the physician If he is known as a regular fellow and foregoes moralizing and attitudinizing the patient finds little difficulty in the discussion of troublesome emotional situations

A practical consideration relative to psychotherapy by the practitioner is the inroad that is made upon time and privacy A single patient with an emotional or situational difficulty may consume a disproportionate amount of time during office hours To give an adequate amount of un *divided attention, the busy doctor must often make a special appointment* after office hours in the evening or over a holiday thus encroaching upon his own relaxation and diversion

A real mental hazard to the practitioner in informal psychotherapy is the captious and often unjustifiable criticism that sometimes emanates from the formal psychiatrist who later deals with the more seriously afflicted patient Hearing only the version of the newly acquired com plainant and not that of the referring physician the specialist is apt to make statements to the patient and his family that are far from tolerant or charitable relative to previous therapeutic devices

Finally, many physicians are discouraged because of their failure to obtain psychotherapeutic results They do not realize that successful treat ment of a profound psychiatric disorder demands as much special skill as a major surgical procedure Often they underestimate the patient s wish to be ill' and his tenacity in clinging to neurotic symptoms In many cases forces are at work which require preservation of the illness and the latter is unconsciously exploited in order to derive secondary advantages which would be dissipated by a cure Thus the matriarch whose heart attack occupies the entire attention of her husband and family (whom she has alienated by other defects of character) would indeed be a disgruntled and neglected object were she to lose her symp toms An older child in the household with an infant might be quite deso late but for the attention derived from an attack of vomiting a belly ache or a tantrum

THE PSYCHIATRIST

It would be impossible to refer to the psychiatrist each patient who suffers from a functional nervous condition The anxiety neurosis *mild depression hypochondriasis and situational* and characterological dif ficulties are the everyday experience of the average practitioner who deals with them to the best of his ability (p 1316) In his routine examination the mental capacities and attitudes are noted The services of the psy chiatrist are sought in dealing with the following clinical problems

1 *The patient suspected of having a psychosis* This is done for the protection of the patient the family the community and the physician
2 *Institutionalization of mental patients* The psychiatrist is an expert in problems relating to institutionalization of the patient *He possesses intimate knowledge of the best type of institutional* care for the individual patient Consultation is mandatory before commitment can be accomplished in most states
3 *Psychometric tests* (p 1325) for the evaluation of mental develop ment where retardation is suspected
4 *Behavior problems among children*

5 *Attempted suicide* (p 1362) Any patient who has attempted suicide should be seen by a psychiatrist
6 *Drug addiction* including *alcoholism* (p 3851)

Psychometric Tests —Psychometric tests are done for intelligence and personality inventories and for diagnosis

Intelligence Tests—The *Army Intelligence* and the *Terman Binet* tests sample a number of different cerebral functions The patient is presented with a list of test items to measure memory reasoning and imagination He is asked to repeat lists of digits define words point out similarities or differences between objects and solve simple problems The score is compared with the scores of typical and different age groups The patient is assigned a mental age (MA) signifying the age group which his performance resembles

By dividing the mental age (MA) by the chronological age (CA) the intelligent quotient (IQ) is obtained The normal IQ is considered as 90 to 110 and includes 60 per cent of the population An IQ of 80 to 89 is considered low and is typical of 14 per cent of our people whereas 70 to 79 is a border line range typical of 5 per cent Only 1 per cent of the people have an IQ below 70 These are classified as feeble minded A range of 50 to 70 is typical for morons 25 to 50 for imbeciles and 0 to 25 for idiots An IQ of 110 to 119 is high and is attained by only 14 per cent of the people From 120 to 129 is superior and reached by only 5 per cent of the population Anything over 130 is found in the highest 1 per cent of all

Since the tests involve various functions it is possible to subdivide the groups and obtain differential measures of memory imagery comparison reasoning comprehension practical judgment ideational judgment sensation and perception of form

The *Kuhlmann Anderson* is a pencil and paper test and can be administered to a group As in the Terman Binet test there is a battery of sub tests measuring arithmetic reasoning vocabulary etc The scores are translated into mental age (MA) chronological age (CA) and IQ (intelligence quotient)

The *Army Alpha* test resembles the Kuhlmann Anderson The *Army Beta* test is a foreign language test for those who do not speak English the *Sequin method* is non language and is employed in the lower levels of intelligence

Personality Inventories—Of the personality inventories the *Bernreuter* is a paper and pencil test containing 125 items The subject is asked to answer yes or no to such questions as Do you day dream frequently? Are you slow in making decisions? Do you heckle or question a public speaker? etc

Through a complicated system of differential statistical weighing four different types of behavior are noted The *BIN* is a measure of neurotic tendency Persons scoring high on this tend to be emotionally unstable A second or self sufficient group prefers to be alone and rarely asks for sympathy and encouragement These tend to ignore the advice of others In the introversion extroversion group persons who score high tend to be introverted they are imaginative and live within themselves Those scor

ing low are extroverted rarely worry seldom suffer emotional upsets or substitute day dreaming for action The last is the dominant sufficient group A high score in this category indicates a tendency to dominate others in face to face situations A low score indicates a submissive tendency The various traits are interrelated and are not independent modes of behavior There is a strong tendency for the neurotic and introvert to go together and a lesser tendency for self sufficiency to accompany dominance

The second type of personality inventory is the *Pressey X C test* which is a paper and pencil exercise containing three groups of words Each group has twenty five lists of five words each In the first group the subject is asked to cross out everything he thinks is wrong or blameworthy In the second he crosses out everything about which he has worried has felt nervous or anxious In the third group he crosses out everything he is interested in

On completing the three groups the subject reviews the list and marks that word in each list from which he has obtained the most reaction The test gives two scores The first is an *affectivity or emotionality score* and involves the total number of words crossed out The second an *idiosyncrasy score* is obtained by noting the number of words crossed out in each line that are not the model words for that line

Diagnostic Tests—Of the diagnostic tests the *Rorschach* is the most interesting It attempts to answer the questions Where does the subject look for his meanings? and What meanings does he find? To test these he is shown a series of standard meaningless ink blots Most of them are black but a few have splotches of color The subject looks at these blots one at a time and tells the tester what they resemble or of what they make him think By studying the reported meanings of these figures the expert gains insight into behavior

The test embodies the principle of a free response to an unconventionalized stimulus If the subject s spontaneous interpretation reflects his way of thinking and living a study of these responses reveals much about the organization of an individual personality and his approach to his environment The *total number* of responses gives an indication of the facility of thinking The *quality* of the responses reflects the intelligence and culture level Some interpret the blot as a whole (scored as a *W response*) indicating a tendency to synthesis and organization Others react to some particular detail (*scored as a D*) *showing an emphasis on the particular and an* inability to synthesize The subject may make a great number of *color responses* (*C*) indicating impulse or affective tendencies The blot may be interpreted in terms of movement (*M*) indicating a tendency to inner life and inner living The relation of *C* (color) to *M* (movement) gives the experience balance which indicates a hypomanic personality If *M* overbalances C it is an evidence of inner living typical of the schizoid

Consideration of the interpretive responses permits the expert to draw positive conclusions regarding the type and level of intelligence the quality and intensity of emotional reaction and the degree of personality integration In the hands of the experienced this seemingly simple device is an interesting and valuable procedure

Other Tests—The *Babcock test for mental deterioration* is based upon

the vocabulary ability By comparing this with other mental processes (such as learning comprehension and repetition) the extent of deterioration may be determined since it has been observed that the vocabulary acuity shows few effects of deterioration whereas other elements in intelligence show more An *efficiency index* is obtained depending upon whether the general intelligence is below or above the norm in relation to vocabulary ability A minus index indicates deterioration

The *Jung Free Association test* tends to uncover what is going on in the patient s mind by recording his responses to a list of common words The tester carefully pronounces each word and the subject responds with the first word he thinks of The associative material often furnishes important clues to the individual thought content In addition to the subject content the lag in response is of importance The subject s reaction time may lengthen with emotional difficulty When a stimulus word is accompanied by a prolonged reaction time it may be taken to indicate that the stimulus words possess some emotional significance for the subject

FORMAL PSYCHOTHERAPY

Within and without the medical profession practitioners of psychotherapy vary between the charlatans who practice faith or mental healing and the trained psychiatrist Unlicensed nervous and mental healers are ubiquitous psychotherapy being the most fertile field for the exploitation of patient and family by the unscrupulous the ignorant and the opportunist The practitioner must acquaint himself with the various cults so that he may guide his patients through the morass of mental illness In this capacity he courts ill will to say the least and possible lawsuits for libel at the worst It is futile to expose the infantile concepts of schools of faith healing or to dissuade a lovesick maiden or sex starved spinster from consulting a particularly virile looking Yogi psychologist astrologer fortune teller palmist or crystal gazer

In proportion to the prevalence of nervous and mental disorders the number of trained psychiatrists in the United States is pitifully small Their ministrations are necessarily time consuming arduous and prolonged and more often than not patients resent being referred to them

The technics of psychotherapy are varied and manifold Many of the skilled and successful specialists employ highly individualized entirely eclectic methods and obtain gratifying results more through dint of personality than methodology The formal therapeutic devices of proven value in the treatment of nervous and mental disorders include distributive analysis hypnosis hypnagogic reverie psychoanalysis shock treatment hyperpyrexia specific therapy and institutionalization To this armamentarium the surgeon has added the performance of pre frontal lobotomy

Distributive Analysis—Distributive analysis formulated by Adolph Meyer is a relatively simple technic of psychotherapy It consists of persuasion reeducation the detailed discussion of the life history confession and ventilation reassurance and guidance It lays emphasis in contradistinction to psychoanalysis on conscious problems and environmental factors It is particularly useful in the psychotherapy of psychotic patients and its relative simplicity makes it applicable to large numbers of psy

chiatric patients It constitutes a more formal and ordered organization of the methods used by the practitioner

Hypnosis—Treatment by hypnosis is a dangerous undertaking except in the hands of the most reputable and expert It should be avoided by the practitioner

Hypno narco analysis (Hypnagogic Reverie)—The exigency of war has confronted psychiatrists with the necessity of treating large numbers of acute neuroses characterized by amnesia Efforts to penetrate the amnesia are made by hypnosis psychoanalysis and the hypnagogic reverie The last is combined technic which incorporates the use of sedative drugs in order to render the subject accessible to hypnotism The exploration of the unconscious is then attempted for purposes of diagnosis and therapy

The hypnagogic reverie may be induced by simple suggestion the use of sedative drugs or the rhythmic auditory stimulus of a metronome The recommended drugs include sodium amytal 0 2 gm orally every three or four hours sodium amytal 0.5 gm in distilled water administered intravenously, pentobarbital sodium (nembutal) injected intravenously at a rate of 1 cc per minute using 2½ per cent solution sodium evipal 0.3 gm orally, sodium pentothal given intravenously as in anesthesia (p 3923) and a combination of scopolamine hydrobromide 0 5 mg with morphine sulfate 15 mg by subcutaneous injection

During the hypnagogic reverie amnesic material is recovered and fully fused with its appropriate emotional content and with normal waking consciousness, the findings are reworked with the patient as he emerges from the hypnoid stage

The hypnagogic reverie involves technics that are too complicated for the general practitioner who need merely be aware of the existence of the method so that he may refer suitable material to the experienced psychiatrist

Psychoanalysis—Psychoanalysis has been the chief impetus in the growing interest in modern psychotherapy So greatly has this important innovation influenced the literature and thinking of our time that it is important to define the procedure and indicate the qualifications that are necessary for its practice

In general the reputable psychoanalyst is a graduate physician who is trained in general psychiatry He has supplemented his medical education with a training analysis by an older and accredited psychoanalyst and has himself analyzed at least a few patients under guidance and tutelage before embarking on his separate career Trained analysts are found only in the larger cities and in limited numbers so that the technic is available to only a minute proportion of the population Self-constituted 'analysts who do not have proper qualifications are to be avoided since inexpert treatment may produce grievous results

It is customary for the patient to recline on a couch so situated that the analyst seated in his chair is beyond the visual field The patient then allows his thoughts to ramble without a systematic presentation of his ideas In this free and aimless fashion symptoms are described the life history and current situational problems emerge and fantasies emotions and dreams are set forth In this way many disturbing ideas and feelings come to verbal expression at the same time the undirected

stream of thought brings to light many deeper connotations and opens the way to an exploration of underlying hidden mechanisms forgotten experiences and buried and troublesome strivings

During these sessions the analyst attempts to keep himself and his personality as much in the background as possible In this way the anal ysis simulates the conditons of the religious confessional in which the priest unseen by the penitent maintains anonymity The analytic pa tient displaces onto his analyst all of the complicated feelings which are entertained relative to those who are important in his real life This shift of feelings to the analyst is called *transference* and it is compounded of love hate fear and all other human reactions expressed in many dis guised forms It is an essential part of the work of the analyst to inves tigate these feelings so that the patient may acquire insight into the un derlying nature of his human relationship

As the analysis proceeds deeper and deeper layers of the unconscious are covered Infantile phantasies are revealed the meaning of symptoms becomes clear incongruous conduct becomes apparent and the emotional tones attached to the *various symptoms are abreacted and dissipated* Generally the mere bringing to the surface of emotionally charged associ ations serves to free the symptoms the patient no longer clings to them their meaning is understood they cease to have an emotional hold and in the successful analysis they vanish

As transference to the analyst constitutes a *substitution neurosis* the final object is to free the patient from the attachment take away the props on which he is leaning and educate him to face the world of reality on his own feet At first the analyst represents the world of reality onto whom the infantile fantasies are attached By degrees the patient learns to shift his interests away from the analyst to the world of objective reality sublimates his energies and learns to face situations in an adult manner A successful analysis then consists of a *reeducation reintegra tion* and *reorientation* of the whole personality The energy is freed and directed into artistic intellectual and moral pursuits thus creating a new goal the patient gives up his neurosis gains a sense of reality from the upbuilding of the real ego and is prepared to meet difficult situations in life in an objective manner

In our limited experience the best results are obtained in the simpler neuroses and conversion mechanisms the profound neuroses and psychoses are little influenced The technic of *psychoanalysis requires attendance for* approximately an hour daily for at least eighteen months *i.e* 400 *sessions* The *fee for each treatment may vary from* 25 an hour At $5 00 an hour 400 sessions cost $2000

Shock Treatment.—The recent innovation or re in the management of the psychoses constitutes peutic advances of the present era *production of a hypoglycemia through* injection of medullary convulsants such as specially devised *electrical equipment* The violence of the convulsions may be jection of *intocostrin* a curare of body weight The total dose should

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stream of thought brings to light many deeper connotations and opens the way to an exploration of underlying hidden mechanisms forgotten experiences and buried and troublesome strivings

During these sessions the analyst attempts to keep himself and his personality as much in the background as possible In this way the analysis simulates the conditons of the religious confessional in which the priest unseen by the penitent maintains anonymity The analytic patient displaces onto his analyst all of the complicated feelings which are entertained relative to those who are important in his real life This shift of feelings to the analyst is called *transference* and it is compounded of love hate fear and all other human reactions expressed in many disguised forms It is an essential part of the work of the analyst to investigate these feelings so that the patient may acquire insight into the underlying nature of his human relationship

As the analysis proceeds deeper and deeper layers of the unconscious are covered Infantile phantasies are revealed the meaning of symptoms becomes clear incongruous conduct becomes apparent and the emotional tones attached to the various symptoms are abreacted and dissipated Generally the mere bringing to the surface of emotionally charged associations serves to free the symptoms the patient no longer clings to them their meaning is understood they cease to have an emotional hold and in the successful analysis they vanish

As transference to the analyst constitutes a *substitution neurosis* the final object is to free the patient from the attachment take away the props on which he is leaning and educate him to face the world of reality on his own feet At first the analyst represents the world of reality onto whom the infantile fantasies are attached By degrees the patient learns *to shift his interests away from the analyst to the world of objective* reality sublimates his energies and learns to face situations in an adult manner A successful analysis then consists of a *reeducation reintegration* and *reorientation* of the whole personality The energy is freed and directed into artistic intellectual and moral pursuits thus creating a new goal the patient gives up his neurosis gains a sense of reality from the upbuilding of the real ego and is prepared to meet difficult situations in life in an objective manner

In our limited experience the best results are obtained in the simpler neuroses and conversion mechanisms the profound neuroses and psychoses are little influenced The technic of psychoanalysis requires attendance for approximately an hour daily for at least eighteen months *i e* perhaps 400 sessions The fee for each treatment may vary from 25 cents to $25 an hour At $5 00 an hour 400 sessions cost $2000

Shock Treatment —The recent innovation or rebirth of shock treatment in the management of the psychoses constitutes one of the greatest therapeutic advances of the present era Convulsions may be induced by the production of a hypoglycemia through overdosage with *insulin* by the injection of medullary convulsants such as *camphor* and *metrazol* and by specially devised *electrical equipment* The danger of fracture due to the violence of the convulsions may be lessened by a prior intramuscular injection of *intocostrin* a curare preparation in a dose of 1 cc to 20 pounds of body weight The total dose *should not exceed 4 cc* See p 1330

The use of these modalities is specialist province under institutional conditions Splendid results have been obtained in *simple depressions* and *manic depressive states* less spectacular remissions are seen in *schizophrenia*

Insulin Shock —For the induction of hypoglycemic shock the patient is institutionalized in a hospital where the staff has become familiar with the technic After a fast of twelve hours the patient is given an initial probatory dose of 15 units of soluble insulin The unitage is increased daily by 5 or 10 units until the signs of hypoglycemic coma begin to appear If coma does not develop three or four hours after the injection the patient is given a solution of sugar to drink if necessary dextrose is injected intravenously

When the induced hypoglycemia reaches the level at which the patient loses consciousness on or about the third hour the unitage is kept stationary and repeated six times weekly for two or three months Each hypoglycemic episode is terminated by giving sugar by nasal tube or intravenous injection A satisfactory response is characterized by loss of consciousness in the third hour and deep coma in the fourth or fifth hour The patient should not be permitted to stay in the deep coma for more than 45 minutes On awakening a substantial meal of carbohydrate is ingested

Metrazol Shock —Metrazol shock is produced by an intravenous injection of 3 to 5 cc of a 10 per cent solution Within 5 to 15 seconds a convulsion is inaugurated The motor response may be so violent as to cause fracture of the jaw or a vertebra In consequence the metrazol convulsion may be eased by the prior use of intocostrin a curare derivative which does not interfere with the convulsion but which softens the muscular response See p 000

If the initial dose of 3 to 5 cc of metrazol is ineffectual the amount is increased each time by 0 5 to 1 cc until the convulsion is produced Metrazol treatments may be given twice weekly it is wise policy to limit the number of convulsions to a total of eight

Electric Convulsive Therapy—Several machines have been developed to apply alternating current to the fronto temporal regions for the production of convulsions Following the passage of the current the patient may have a minor or major seizure with loss of consciousness for a few minutes Intocostrin may be used (p 1329) to prevent injury due to the violence of the seizure or preferably the treatment may be given after intravenous anesthesia with sodium amytal 0.5 gm (7½ grains) (in 10 cc of diluent)

Following the electrically induced convulsion the patient is restored to consciousness in 30 to 35 seconds and usually exhibits no after effects other than some amnesia Electric convulsions may be given twice weekly for a total of eight to twelve treatments

Hyperpyrexia —The use of induced fever has proven a therapeutic boon particularly in the treatment of *general paresis* of syphilitic origin The state of hyperpyrexia is induced through artificial infection with tertian or quartan *malaria* through intravenously injected *foreign protein* (typhoid vaccine) or by mechanical devices such as the *hypertherm*

These therapeutic measures are specialist province and not without danger even under optimum conditions

Specific Treatment —The organic psychoses of specific origin are treated by methods directed at the fundamental etiologic mechanism Thus syphilis of the nervous system is attacked by anti syphilitic drugs and the psychoses that result from avitaminosis require the feeding or injection of the necessary metabolic agencies (p 1375)

Institutionalization —In general the practitioner recommends institutionalization for those whose illnesses preclude their useful function in the community or who are destructive of their own their family and community interests

The practitioner must inform himself concerning the *medicolegal technicalities* that arise in the institutionalization of patients These formalities differ in the various states Local regulations may be obtained from police or legal authorites and a few well directed inquiries may save the practitioner a great deal of criticism trouble and even litigation

Neurological and psychiatric hospitals vary between the splendid reliable humane and scientific establishments (altogether too few in number) and the neurological boarding hou es run by charlatans and incompetent or unethical practitioners

It is often a matter of considerable difficulty to persuade relatives to commit the psychotic The resistance is usually greatest in dealing with mental disorders that involve children or elderly parents Often many lives are affected and even ruined by the insistence of the family that the afflicted must not be put away Tremendous economic sacrifices are made to maintain the patient in an incompetent private santiarium when far better provision could be afforded in a municipal state or federal institution supported by the taxpayer

Pre frontal Lobotomy —The operation of pre frontal lobotomy has been devised in an effort to deal with the psychoses Holes are drilled in the skull and the thalamo frontal radiation is severed with a leukotome passed through a cannula In expert hands the procedure is not dangerous and an occasional spectacular result has been obtained in deteriorated psychotics who have failed to respond to all other types of therapy The most favorable results are reported in obsessive tension states hypochondriasis and agitated depressions

CHAPTER 63

PSYCHIATRY MENTAL DEFICIENCY

IDIOCY imbecility and moronity are the three levels of feeblemindedness See *Psychometric Tests* (p 1325)

Idiocy —An idiot is a person with a mental age of two years or less and an intelligence quotient between 0 and 30 Idiots are unable to care for themselves even to the extent of dealing with common physical dangers In a sense they are more like animals than humans They can utter but a few monosyllables and are frequently unable to walk

Imbecility —The imbecile has a mental range of from three to seven years and an intelligence quotient that varies between 30 and 50 Imbeciles are incapable of managing for themselves on anything beyond the most primitive level They can learn simple toilet habits and are capable of feeding themselves but beyond these functions they are quite helpless

Moronity —The moron has a mental age of from seven to twelve years and an intelligence quotient that varies between 50 and 70 Moronity does not constitute so striking a deviation as idiocy and imbecility Moronity may escape attention until schooling begins and the backwardness is discovered through the failure of the subject to learn and progress

Management —The management of the feebleminded child poses a difficult problem for the practitioner Under no circumstances should he attempt to render any judgment without the assistance of the expert A complete neurologic and psychiatric examination is mandatory *Psychometric tests* (p 1325) are performed the disposition of the child depends upon the findings translated into terms of emotional social and economic factors in the household situation

There is obviously no specific form of therapy that can be employed It becomes necessary to confront parents with a realistic view of the situation and assist them in making an adjustment for the unfortunate child and themselves The practitioner attempts the difficult tasks of protecting the child getting the most out of the handicapped life and preventing bewildered and well intentioned parents from ruining several lives in a futile effort to save one The continued presence of an idiot or imbecile in a home may result in financial sacrifices on the part of the parents the exertion of a deleterious influence on other children growing up in the household and a complete submersion of all other activities to the protection of the hopelessly handicapped child

Institutionalization —There is little doubt that institutionalization furnishes the best outlook for idiots and imbeciles This advice always meets with the most violent resistance particularly on the part of the mother

DIFFERENTIAL DIAGNOSIS OF

Feeblemindedness

The suspicion of feeble mindedness warrants specialist consultation with the trained neuropsychiatrist. On rare occasions therapy may be initiated with some small hope of success but in all instances the practitioner owes it to him elf to be protected against criticism in the face of these *overwhelming tragedies*

CAUSE	DIAGNOSTIC FEATURES
Cerebral Birth Trauma	Spa ticity palsy and atheloses (p 2771)
Erythroblastosis Foetalis	Icterus gravis Hemolytic anemia due to abnormalities of the Rh factor
Mongolian Idiocy	Characteristic obliquity of eyes (p 2774)
Microcephalus	Early closure of fontanelles and small circumference of head (p 2774)
Cretinism	Thickening of skin protrusion of tongue and umbilical hernia Responds to thyroid extract (p 1191)
Hydrocephalus	Pumpkin Head Refer to neurosurgeon for possible palliative procedure (p 2774)
Cachexia	In chronic disease particularly tuberculosis endocrinopathies and malignancie
Congenital Syphilis	Positive serologic findings in maternal umbilical and infant s blood (p 2787)
Anencephaly	Absence of brain
Porencephaly	Defects of cerebral hemispheres (p 1407)
Cerebral Agenesis	With palsies ataxia and cranial nerve invol e ment (p 1408)
Amaurotic Family Idiocy	With characteristic cherry red spot in fundu (p 1412)
Niemann Pick Syndrome	Anemia leukocytosis splenomegaly and hepatomegaly (p 1134)
Hand Christian Schuller Syndrome	Diabetes insipidus exophthalmos and defects of bone (p 1137)
Laurence Moon B edl Syndrome	Obesity hypogonadism retinitis p gmentosa and polydactyli m (p 1166)
Tuberous Sclerosis	Associated with cutaneous pigmentation adenoma sebaceum and fibromas (p 1133)
Huntington s Chorea	Familial disturbance associated with motor disturbances and mental deterioration (p 1417)
Progressive Lenticular Degeneration	Athetosis spasmodic laughter and hob-nail cirrhosis of liver (p 1418)
Aplasia Axialis Extracorticalis Congenita	With nystagmus headache and speech defects (p 1418)

In some instances her revulsion is justified since many public institutions for the care of the feebleminded are overcrowded understaffed and thoroughl unsatisfactory The better private schools are exceedingly expen

sive and quite beyond the budgetary possibilities of all save those in the upper income brackets

One of the principal uses of the psychiatrist is to obtain his broader knowledge of the local institutions conducted by private enterprise and those which operate under the auspices of the state It may here be stated that it does not necessarily follow that the more expensive excel those whose costs are more moderate Often the retreats supported by the tax payer enjoy facilities that are far superior to those under private management

At times it is necessary for the physician to assist the parents in their attempts to keep the child at home He understands that there are imponderable emotional aspects feelings of guilt and other unconscious attitudes that lead parents determinedly to oppose institutionalization of the deficient child If the necessary sacrifices are not excessive it may be wiser to permit the child to remain at home at least temporarily If an extremely modest goal is set for the mentally deficient child the afflicted youngster may function in a socially acceptable manner and may master simple tasks More ambitious goals lead to inevitable disappointment Drastic treatments by shock fever or lobotomy have no promise for benefit

The administration of 8 to 10 gm (120 to 150 grains) of glutamic acid appears temporarily to raise the intellectual levels of non epileptic mental defects

CHAPTER 64

PSYCHIATRY: THE NEUROSES

- Etiology of the Neuroses
- Psychoanalytic Concept of the Origin and Pathogenesis of the Neuroses
  - The Unconscious and the Libido
  - Depth Psychology (Ego, Id and Superego)
  - Ego and Death Instincts
  - Pleasure-pain and Reality Principles
  - Repression and Resistance
  - Conflict
  - Results of Conflict
  - Determination of the Nature of the Reaction
  - Precipitating Factors
  - The Complex
  - The Reactions to Conflict and the Complex
  - Terminology of Neuroses
- Symptoms of Neuroses
  - Anxiety
  - Phobias
  - Neurasthenia
  - Hypochondria
  - Conversion
  - Fixations and Regressions
  - Compulsion
  - Perversions
  - Displacement, Projection and Rationalization
  - Dreams and Slips of the Tongue
- Resolution of the Neuroses
  - The Latent Neurosis
  - The Useful Neurosis
  - The Clinical Neurosis
- Clinical Varieties of Neuroses
  - The Anxiety Neurosis
  - Neurasthenia
  - Hypochondriasis
  - Conversion or Transference Neuroses (Hysteria)
  - Traumatic Neuroses
  - Compensation Neuroses
  - Neuroses of Regression and Perversion
  - Mixed Neuroses
- Disorders of Total Personality
  - Personality, Behavior and Conduct Disorders

THE neuroses have been previously defined as psychological disturbances which arise as reactions to stress; they are not accompanied by any serious alteration in evaluation of reality and are partial reactions in that the personality is otherwise well integrated and socially organized.

The neuroses are of such common frequency that many practitioners believe that neurotic behavior is ubiquitous. Neurotic symptoms usually enter the realm of clinical medicine only when the patient is sufficiently disturbed to seek consultation with his physician. However, it is the re

sponsibility of the physician to recognize the existence of a neurosis which the patient may attempt to conceal through ignorance or cowardice Acuity of insight and tact on the part of the family practitioner are vital forces in the earlier recognition and treatment of the neurosis years before the patient may recognize the need for assistance Preventative psychotherapy is of as great value and significance as prophylactic immunizations in the infections

ETIOLOGY OF THE NEUROSES

Until the time of Freud the etiology of the neuroses was obscure and investigations failed to lead to any satisfactory therapeutic approach to the management of the afflicted It was generally believed that *hereditary* and *constitutional factors* were of considerable importance since familial examples were the rule Organicists pursued the possibility that the neurosis resulted from subtle and undemonstrable molecular and pathologic changes in the nervous system possibly resulting from prenatal influences syphilis in the third and fourth generation congenital afflictions birth trauma intra uterine infection abortive infections involving the meninges or brain tissue proper and sequels of the exanthemas or vascular abnormalities

Zealous *reformers* attributed the neuroses to excessive or long standing indulgence in alcohol to masturbation or to sexual excesses or sexual abstinence *Physiologists* claimed the affliction resulted from disorders in nerve impulse production and the *endocrinologists* believed that the psychiatric disorder rested upon a dislocation in the interplay of the glands of internal secretion The *gynecologists* clung to etymology and since hysteria is derived from hystera (womb) they corrected uterine malpositions and removed the womb often with a temporary and illusory psychotherapeutic result but with a later profound rage and depression Advocates of the theory of *auto intoxication* sounded their drums particularly in the elucidation of the depressed states and psychasthenia The enthusiasm for *focal infection* led to a wave of tonsillectomies appendectomies cholecystectomies tooth extractions and wholesale removals of the large intestine—all to no good or permanent purpose Students of the *involuntary nervous system* attempted to correlate the vegetative neuroses and psychiatric disturbances and while it is true that these coexist it is more likely that both arise from a common stem than that either one primarily causes the other

It remained for Freud to lift the curtain of obscurity and suggest a working hypothesis for the origin of the neuroses His theories and investigations have a rational appeal and a therapeutic approach that hold some promise for benefit to the patient Stated in broadest terms it is Freud s belief that there is a purposive nature to the neurosis the symptoms are not meaningless and psychological factors of repression conflict and persistent infantile behavior patterns figure prominently in the etiology The manifestations serve as a defense against the gratification of unconscious repressed guilt laden desires They represent disguised gratifications of repressed strivings which cannot be permitted conscious expression

The psychoanalytic therapeutic endeavor depends upon the *replace*

ment of conscious deeds for unconscious mental acts The Freudian theory of pathogenesis and treatment are further enlarged in succeeding para graphs

PSYCHOANALYTIC CONCEPT OF THE ORIGIN AND PATHOGENESIS OF THE NEUROSES

There is universal agreement that the faculties of thought and idea tion reside in the cerebrum Prior to the time of Freud the processes of voluntary cerebration were recognized and abnormalities were catalogued without recognition of a possible relationship between sanity and in sanity The writings of Freud have emphasized the levels of conscious ness the conscious is that portion of our reasonable being which deals with objective realities the preconscious a subliminal state through which unconsciously motivated ideas must pass in order to reach con sciousness

The Unconscious and the Libido—The unconscious is a *dynamic force* in which are stored the experiences of the lifetime of the individual They are often charged with emotion and exist not in a quiescent state but in a flux much as the contents of a boiling cauldron or a smouldering volcano All instinctual energies converge to form the *libido* The sexual and aggressive components of the libido are most important since they are most apt to produce conflict with society conscious conscience or fear

The great contribution of Freud has been his assumption of subcon scious or unconscious mental processes and his insistence that these are no mere passive devices but rather dynamic influences in the determina tion of personality dream life conduct behavior and the nervous and mental disorders of clinical practice The study of the science of uncon scious mental processes has been termed by Freud *depth psychology*

Depth Psychology (Ego Id and Superego)—Freud regards the mental apparatus as a composite instrument It is made up of a *superficial conscious stratum* concerned with the perception of the external world and a *deeper unconscious* the reservoir of instinctive impulses Conscious and unconscious are possessed of three major components to which Freud has applied the terms Superego Ego and Id The Superego is the con science processes the Id represents the instinctual energy reservoir and the Ego is that aspect of personality which relates the individual to the external world by perceptual and affector mechanisms Mental processes are derived from the interplay of forces which assist or inhibit one an other combine or enter into compromises one with the other

This Freudian concept of the dual or manifold aspects of the human mind is acceptable to thinking physicians Indeed the hypothesis is neither new nor unique so far as Freud is concerned since the concepts of man wrestling with his soul and the portrayal of sacred and profane love have been current in the literature and art of the world since history has been recorded

Ego and Death Instincts—The dynamic depth psychology of Freud re gards the unconscious as the reservoir of instinctive impulses It is as sumed that the latter include ego and death instincts

The *ego instincts* are directed toward self preservation hence their concern is with the procreative functions Freud has given the name

libido to the forces of eros It is in the elucidation of this ego instinct" that Freud has suffered most from his critics and overzealous devotees On even the most superficial inspection it is apparent that the Freudian libido represents a great deal more than mere sexual intercourse In its broader significance and in the sense that Freud originally intended the libido is concerned with all factors which integrate for racial self preservation Whereas copulation between male and female constitutes a necessary link in the chain of events there is no disposition in the Freudian psychology to state that the only concern of the libido is relative to sexual union and of itself

Freud also recognizes in the human mind an instinct for destruction which tends toward the dissolution of what is living This *death instinct* not accepted by all psychoanalysts is an outstanding characteristic of many individuals and of certain national traits of the Nazis and the Japanese

It was Freud s belief that instincts had aims or ways of gratification and objects individuals or things towards which the instinct was directed as a goal

Pleasure pain and Reality Principles—It is the psychoanalytic concept that instincts have a definite charge ' It is the function of the mental apparatus to hinder any damming up of energies and to keep as low as possible the total amount of excitation to which it is subject The course of the mental process is automatically regulated by the *pleasure-pain principle* Pain is related to an increase of excitation and pleasure to a decrease In the course of its development the original pleasure principle undergoes a modification with reference to the external world It gives place to the *reality principle* whereby the mental apparatus learns to postpone the pleasure of satisfaction and to tolerate temporarily feelings of pain

Repression and Resistance—In the world of reality the mind is required to exercise the function of censorship over the fundamental instincts It is necessary to exclude from consciousness and from any influence upon conduct those tendencies which displease the conscious mental processes The exclusion of these tendencies constitutes a *repression* The repressed instinctual impulses are not made powerless but they succeed in making their influences felt by circuitous paths and the indirect or substitutive gratification of repressed impulses These devices constitute the symptoms of the neurosis and when the physician attempts to bring these repressions into the patient s consciousness he provokes a *resistance*

Conflict—Since there exists a dynamic unconscious which constitutes the reservoir of instinctive impulses it is inevitable that these should come in conflict with objective reality whose concerns are the artificial barriers that are set up in the external world The infant cannot urinate whenever its bladder is full it cannot defecate merely because the rectal ampulla is stimulated but must wait for an appropriate time and an appropriate place Its instinct is being opposed by conformity to manmade standards The subconscious is at grips with the conscious and the id is being dominated by the superego These divergencies give rise to *conflict* The individual personality his ego-structure with its strength and weaknesses and its compulsive patterns of behavior is hammered out by

the powerful interactions between instinctual forces external reality and the conscious and unconscious conscience of the super ego

Results of Conflict —The results of conflict manifest themselves in normal and *abnormal human behavior* The individual exhibits love hate wishes desires compulsions fears anxiety perversions fixations transferences displacement identification rationalization sublimation dreams and conversion Each and all of these are *compatible with the norm* provided that the life love and occupation of the individual are not seriously affected When they involve only a portion of the personality without a change in the reality situation when the patient retains an insight into *his affliction although the symptoms* begin to interfere with the enjoyment of life or its accomplishments the condition is to be regarded as a *neurosis*

When there is total involvement of personality a quantitative change in reality a regression to primitive levels of behavior with lack of insight and when the direct verbal expressions are the language of the unconscious with delusions hallucinations and disorders in the form and flow of thought the patient is then regarded as being *psychotic* These definitions and differentiations are considered in more detail in succeeding paragraphs

Determination of the Nature of the Reaction —One of the unsolved problems of psychiatry is the elucidation of the factors which are responsible for individual and normal behavior Why does one patient develop an anxiety another hypertension the third a gastric neurosis and still another a psychosis? This same problem is inherent in the mechanisms that produce *the reaction picture* of autonomic imbalance Present information holds no answer to the problem Many of the psychoanalytically trained practitioners regard the nature of the disturbance as the predominating factor Thus it is thought that the type of conflict determines whether the patient is to develop a gastric neurosis or a retentive or expulsive type of intestinal neurosis The theories which have been put forth relative to this point are far from conclusive though no better explanation is today available

Precipitating Factors —It is quite possible for the neurosis to lie dormant Conflict is present but like a quiescent volcano is apparently in a state of inactivity though closer scrutiny reveals the turbulent undercurrent

The *dormant neurosis* is often precipitated by nonspecific exciting causes and then unfortunately the clinical diagnosis intimates that the secondary factor was actually primary Thus the literature speaks of the "traumatic neuroses war neuroses *compensation neuroses* menopausal and pregnancy neuroses and adolescent neuroses These terms are misleading since they stress the less important mechanisms and cloud the significant disturbances

The Complex —The result of conflict is the development by the patient of a complex which Freud defines as an unconscious group of ideas charged with various emotions These complexes indirectly influence normal behavior and often produce inexplicable symptoms Two of the more frequently encountered complexes are described by the psychoanalysts as the castration and Oedipus syndromes

Castration and Oedipus Complexes —The *castration complex* represents an infantile phantasy concerning the loss of or threat to the phallus The

Oedipus complex embodies an identification of the child with the parent of the same sex and a hostile intent against that parent with the objective of displacing him or her in the affection of the parent of the opposite sex

The Reactions to Conflict and the Complex—The reactions of the individual to the complex that arises from conflict are varied The conscious ego which acts as a 'censor' to the subconscious id" may successfully repress the baser impulses The mechanism of repression however is no mere erasure since the complex is held in the dynamic unconscious under pressure It becomes charged with emotion and exists in a flux not in a quiescent state

Terminology of Neuroses—It was Freud s belief that the most intense repressions fall upon the sexual and aggression instincts The repressed libido responded clinically in a variety of ways including the development of neuroses These were capable of subdivision into those which constituted *simple repressions* those characterized by the mechanisms of *conversion* or *transference* and the *regressions* and *perversions*

The principal value of the Freud classification is the grouping of the neuroses on the basis of dynamic mechanisms A more useful arrangement is one which merely groups the more frequent symptom complexes and recognizes (*1*) Neuroses in which anxiety predominates (*2*) those in which there are predominately conversion symptoms (*3*) neuroses characterized by obsessional and compulsive phenomena (*4*) the addictions and perversions which may occur in association with any of the previous varieties

The Simple Neuroses (Actual Neuroses)—Before embarking further into the discussions of the neuroses it becomes necessary to clarify terminology The present usage is to include in the simple neuroses the conditions that are variously described as the *anxiety neurosis neurasthenia* and *hypochondria* They correspond to what Freud calls the actual neuroses

Conversion or Transference Neuroses (Psychoneuroses)—The conversion or transference types of neurosis are called the psychoneuroses by Freud and are subdivided into *conversion* and *anxiety hysterias Occupational* and *war* neuroses are included in the conversion category It is the present purpose to avoid the use of the term hysteria since it has confusing and disturbing connotations It is resented by the laity who regard it as synonymous with malingering exaggeration and thoroughly culpable conduct disorders

Regressive Neuroses and Perversions—The regressive and perversion neuroses constitute the most serious types Included in this group are the *compulsion neuroses* the *obsessional neuroses* and the *perversions*

SYMPTOMS OF NEUROSIS

The common symptoms of neurosis include anxieties phobias neurasthenia hypochondriasis compulsion obsessions conversions and perversions

Anxiety—Anxiety is the most common neurotic symptom It occurs in the anxiety neurosis in anxiety hysteria in the phobias hypochondriasis melancholias compulsions and obsessions The anxiety may be referred to death disaster heart failure suffocation insanity cancer apoplexy coro-

nary thrombosis continued virginity or imminent rape The symptoms occur by day or night An annoying characteristic is the *pavor nocturnus* or horror which may or may not be associated with the nightmare

Anxiety symptoms are most common in the young and occur more frequently in females As objective accompaniments and results of anxiety there appear tachycardia elevation of blood pressure vasodermal phenomena such as blushing or blanching perspiration urination diarrhea vomiting and cardiac irregularities These phenomena in the acute phases give rise to serious diagnostic problems Accurate interpretation requires careful and repeated observation over a period of time

Phobias—The phobias are hysterical fears with a definite ideational content They constitute according to the Freudians an unconscious wish or emotion that has become dissociated from a more vivid desire The virgin who has a fear of men (androphobia) is probably highly desirous of male companionship and anticipates sexual gratification Other instances of phobia seem less clearly defined and many have been labeled by the descriptive school of neurologists (p 1336)

Neurasthenia—Neurasthenia constitutes an abnormal fatigue and resultant exaggerated irritability It occurs most often in the middle aged but it may be experienced by the young Patients complain of tiring weakness fatigability inability to concentrate memory defects pressure on the head pain in the back dizziness asthenopia orthostatic tachycardia and excessive sensitivity to light noise odors or taste The neurasthenic symptoms are often associated with a subnormal temperature low blood pressure low blood sugar tachycardia and more often than is generally suspected a low basal metabolic rate

Often the neurasthenic gives a history of increased sexual desire with excessive sexual activity and inadequate sexual gratification As a result the complaints include chronic masturbation nocturnal emissions spermatorrhea futile erections premature ejaculations and impotence The last occurs at the time of greatest sexual excitation and the optimal opportunity for gratification Of all the neuroses neurasthenia is most likely to progress to schizophrenia and its recognition demands psychiatric consultation

Hypochondria—Hypochondria indicates a morbid preoccupation with organ integrity When it becomes delusional it is an integral part of the psychotic reaction most frequently however it is a generalized frame of mind an incessant worry and half conviction that something is wrong Most often the attention is focused on the erotic zones such as the mouth anus and genitalia Hypochondriasis may be observed in males but is more common in females at the time of the menopause

Conversion—The conversion symptoms constitute the greatest problem in the neuroses and represent the various manifestations of hysteria The variety of the conversions is as manifold as that of the human countenance and the finger prints No two individuals seemingly manifest the same conversion symptoms yet each complex is unique for that particular individual

The repertoire of conversions include sensory motor autonomic visceral psychic and emotional manifestations

Pain—Pain is a frequent conversion symptom and one which gives rise

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or emotional disturbance The psychiatrist dared not trespass upon the field being warned off by the visible ulceration of the mucous membrane Meantime the gastro-enterologist intent upon healing of the ulcer became focused upon gastric acidity gastric intubation and lavages with only lip service to the psychogenic disturbance

Developments in the field of *psychosomatic medicine* emphasize the concept of the unity of body and psyche and of their constant interrelationship It is truism old in medicine but recently reemphasized that illness involves the indicated organ and the entire personality In addition to specific emotional factors implicated etiologically in organic illness the reaction of the individual to his illness requires understanding The patient s neurosis may complicate or contribute to the etiology of his disease and on the other hand the organic disease may be exploited neurotically

Essentially the functional theory of organic disorders is the recognition that diseases are caused by internal as well as external factors Franz Alexander* a pioneer worker in the field of psychosomatic relationships asserts Many chronic disturbances are not caused by external mechanical chemical factors or by the micro organisms but by the continuous functional stress arising during the everyday life of the organism and its struggle for existence Fears if repressed result in permanent chronic emotional tensions which disturb the functions of the vegetative organs Many emotions due to the complication of our social life cannot be freely expressed or relieved through voluntary activities but remain repressed and then are diverted into wrong channels instead of being expressed in voluntary innervations without influencing internal vegetative functions such as digestion respiration or circulation There is much evidence to show that just as pathological microorganisms are specific and have a certain affinity to certain organs so also emotional conflicts are different and are liable in accordance with these differences to involve different internal organs inhibited rage seems to have a specific relationship to the cardiovascular system dependent help seeking tendencies seem to have a specific relationship to the functions of nutrition again different and specific conflict betwen sexual wishes and dependent tendencies seems to have a specific influence on respiratory disturbances The increasing knowledge of the relations of emotions to normal and disturbed body functions requires that for the modern physician emotional conflict should become just as real and tangible issues as visible microorganisms

With the more recent popularization of psychogenic factors in clinical medicine an attempt has been made to unite the efforts of the organicist treating the end organ manifestations and the psychiatrist interested in the emotional factor This wedding has been legitimatized under the title of Psychosomatic Medicine

The enthusiasts for psychosomatic medicine must not be permitted to go to the extreme of isolating their specialty The present delineation holds that the psychosomatic manifestations are essentially conversions and hence not different in their origin implications management and treatment than the neuroses without objective evidences of somatization Psychosomatic implications are considered in the present text in the presentations of the following disturbances

* Psychological Aspects of Medicine Psychosom Med 1 7-18 (Jan) 1939

to great difficulty in diagnosis (p 1474) The more frequently observed painful hysterical afflictions are the *clavus headache* often characterized by a boring sensation in the skull, *coccygodynia* discussed more fully in the section on back pain (p 3072) and *mastodynia* and *glossodynia* which often have erogenous implications

Paresthesia—The conversion paresthesias are characterized by absence of objective sensory findings bilateral and symmetrical distribution and failure of the complaint to correspond to the anatomic distribution of the nerves Thus there are encountered *pruritus* particularly in erogenous zones (vulva vagina rectum) *acroparesthesias, hemianesthesias,* sock and glove' *anesthesia* and *hemianalgesias* In the special senses patients note *anosmia amaurosis photophobia myopia micropsia macropsia* and *mutism*

Abnormalities of Striated Muscle—The conversion abnormalities of muscle take the forms of *spasm or paralyses* There occur peripheral *tics* and *tremors contractures* isolated *muscle spasms* and *astasia abasia* *Peripheral paralyses* occur without changes in the reflexes They may be in the nature of *monoplegia hemiplegia* or *paraplegia* In the realm of the special senses there are observed *blepharospasm pseudoptosis glossolabial paralyses stammering stuttering* and *aphonia*

Autonomic Manifestations— Autonomic imbalance frequently accompanies other of the conversion symptoms *Vasodermal disturbances* are observed as blushing flushing blanching suffusion and moisture of the extremities or the more disturbing manifestation of the cold clammy hands and feet The *cutaneous phenomena* include dermagraphia urticaria angioneurotic edema and the maddening and perplexing varieties of pruritus involving all skin surfaces but more often the anus vulva vagina or rectum

The vegetative disturbance may be reflected in the internal viscera There are thus produced the *gastric and intestinal neuroses* globus hystericus aerophagia cardiospasm anorexia nervosa bulimia pica nervous vomiting borborygmi diarrhea (mucous colitis) and obstinate constipation *Genito urinary manifestations* include vaginismus enuresis perineal spasms, pollakiuria (frequent voiding) urinary retention and pseudocyesis (false pregnancy)

The *cardiovascular neuroses* include instability of the pulse rate or rhythm hypertension hypotension lability of the blood pressure tachycardia cardiac irregularities and peripheral vascular spasms The respiratory symptoms may be tachypnea sighing gasping and the familiar inability to catch the breath The existence of hysterical fever' is possible aside from malingering

Visceral or Psychosomatic Manifestations—Psychogenic disturbances also may produce somatizations in which there are objective evidences of pathologic disturbance in the afflicted organ These clinical manifestations formerly constituted a no man s land Psychiatrists avoided trespassing upon the fields of organic disease Organicists in clinical medicine treated the local manifestation neglecting the psychogenic overtone Each patient became a battleground of divergent medical opinion Thus the patient with peptic ulcer was recognized as suffering from emotional instability Often the onset of gastric symptoms was directly related to a psychic

Regression —In the regression the libido having developed along normal lines returns or reverts to an earlier point of fixation These situations of greater gravity occur in every neurosis but particularly the compulsive and obsessive neuroses psychasthenia and the perversions The prognosis of regressions is graver and treatment less satisfactory

Compulsion —*The compulsion constitutes an irrepressible urge to carry* out what is apparently a needless and purposeless activity Thus the sufferer washes his hands indefinitely turns off lights carries out repetitive rituals involving unnecessarily strict attention to orderliness and tidiness and is occupied with all manner of superstitions and fetishes There is the necessity to touch wood avoid or walk on cracks in the pavement carry a lucky piece or charm and observe certain curious superstitions and rituals *In more extreme degrees the patient develops such manias as klepto*mania (stealing) toxicomania (compulsion to take medicine) dipsomania (the compulsion to drink) pyromania (compulsion to set fire) and trichotillomania (compulsion to pull out hair)

Perversion —The perversions are compulsions towards some abnormal form of instinctual gratification Often there is any one or more of the following sexual disturbances continued and chronic masturbation maso*chism sadism exhibitionalism or homosexuality Perverts indulge in such* practices as pederasty cunnilinguism fellatio bestiality incest and necrophilia See pp 2409 2491

Displacement Projection and Rationalization —More complicated disturbances of the libido result in *displacement* and *projection* The former indicates a detachment of emotions from the objectionable idea and an attachment to some other less obvious or less objectionable object or person Thus the child with an unconscious homosexual urge develops a crush on a teacher of the same sex Projection implies that the repressed idea is *regarded as belonging to another person* Displacement and projection are used constantly by every human being in the formation of dreams and fantasies They become the instruments of illness when they begin to cause overt difficulties and are most commonly seen in the psychoses *Rationalization* consists in utilizing the unconscious in order to give plausibility to incongruous ideas

Dreams and Slips of the Tongue —Beside clinical symptoms Freud believes that neurotic conflict reflects *itself in dream life and in slips of the* tongue In the former the disturbance dramatizes itself through symbol*ization of a bewildering character In the course of* psychoanalytic therapy the significance of these symbols and the seemingly innocent lapses in speech permit the trained observer to interpret their significance in terms of individual conflict

RESOLUTION OF THE NEUROSIS

It is inevitable that each life should involve conflict The manifestation may be latent useful or harmful

The Latent Neurosis —*In the vast majority of individuals the conflict* never becomes clarified It exists often like a birthmark as an accepted *character trait or* at worst as a nuisance which annoys the patient but does not seriously interfere with his life Thus an anxiety or a phobia per

Psychosomatic Disturbances

The Digestive Tract
- Cardiospasm
- Anorexia nervosa
- Plummer Vinson syndrome
- Peptic ulcer
- Regional ileitis
- Nonspecific chronic ulcerative colitis
- Mucous colitis

The Circulatory System
- Essential hypertension
- Neurocirculatory asthenia (soldier s heart effort syndrome)
- The arrhythmias

The Tegumentary System
- Urticaria
- Angioneurotic edema
- Neurodermatitis
- Acroparesthesia
- Acrocyanosis
- Erythromelalgia
- Dermatitis factitia
- Infantile eczema
- Alopecia

The Respiratory System
- Vasomotor rhinitis
- Bronchial asthma

The Urinary System
- *Enuresis*

The Ductless Glands
- Hyperthyroidism
- Simmonds disease
- Diabetes mellitus
- Hyperinsulinism
- Obesity

The Gonads
- Dysmenorrhea
- Amenorrhea
- Premenstrual tension
- Frigidity
- Impotence

The Voluntary Nervous System
- Migraine
- Epilepsy
- Asthenopia

Psychic and Emotional Disturbances —Conversion symptoms may involve psyche and emotions Not infrequently patients develop automatism amnesia catalepsy trances clouding of consciousness lapses in consciousness narcolepsy somnambulism fugues delirium dream states stupor dual personalities and particularly disturbances in sexuality such as frigidity impotence nymphomania and satyrism Hysterical convulsions may assume the *passionate attitudes* mimicking sexual acts Abnormal moods occur as the *Ganser syndrome* in prisoners

Fixations and Regressions —Besides conflict and conversion Freud recognizes mechanisms of fixation and regression the clarification of which requires a preliminary statement of his views relative to the sexual instinct

The Development of the Sexual Instinct —Freud believes that the sexual instinct initiates at the beginning of extra uterine life and reaches a first culminating point (*early period*) at or before the fifth year The early period is followed by a *period of latency* in which the sexual instinct is inhibited or interrupted until the age of puberty when there is a *second climax* of development until normal gratification occurs Freud holds that the experiences of the early period of childhood in combination with the inherited sexual constitution form the disposition for the subsequent development of the individual character or the manifestations of his neuroticism

Repression and Fixation —When the sexual instinct is repressed the libido becomes arrested at some stage of infantile development The arrest of the libido in the early stage of development is termed a *fixation* Since masturbation and auto erotism characterize the infantile state the neurotic manifests these types of reaction and an infantile narcissism with preoccupation referable to oral and anal zones

The Anxiety Neurosis

There is a certain amount of anxiety that accompanies each medical condition and which persists throughout the course of the affliction The realm of the anxiety neurosis however is approached when the amount or duration of the anxiety is disproportionate to the cause when it dominates the clinical symptomatology interferes with the patient s well being and progress and impedes favorable progress

Clinical Manifestations—The anxiety neurosis is the commonest of all clinical derangements It may be acute approaching a panic state and it may be chronic or recurrent Anxiety symptoms may bear a repetitive pattern and the patient recurrently suffers from cancer blood poisoning lockjaw apoplexy or acute indigestion More often the panic states run the gamut from kidnapping through murder suicide malignant disease or grave infection

Provocative Cause—The anxiety may be precipitated by a tangible symptom or physical finding or it may result from a disturbing dream or from seemingly no cause whatsoever The patient with headache develops anxiety about a brain tumor meningitis or encephalitis A scratch causes fear of septic blood poisoning or tetanus a sebaceous cyst is regarded as cancerous and precordial pain as indicative of coronary thrombosis

At times the anxiety is unassociated with anything tangible and is based on *projections into the future* The housewife whose husband is delayed anticipates that he has been killed and that her child who has lingered on the way home from school has been kidnapped Each occurrence no matter how trivial or inconsequential has an affect of sufficient intensity to warrant the assumption that a major tragedy has occurred

Anxieties occur as vividly in *dreams* as in reality situations Characteristic of dreams is the *pavor nocturnus* in which the patient wakens suddenly in the midst of sleep with overwhelming and distressing anxiety symptoms Often the provocative dream is forgotten or repressed At times the panic state arises without apparent provocation in conscious cerebration or dream life In all likelihood many of these situations are conditioned by the sound of a voice an odor or a visual or tactile sensation repressed from consciousness

Autonomic Imbalance—The anxiety neurosis rarely occurs without accompanying disturbances in the realm of the psyche and the involuntary nervous system The patient almost invariably has other emotional difficulties and is usually troubled by a sense of insecurity and inadequacy especially as compared to self inflicted overconscientious standards More disturbing for the diagnostician are the autonomic accompaniments of anxiety since they *simulate organic disease* The acute panic is accompanied by tachycardia sweating pallor flushing shortness of breath feelings of suffocation choking sensations urgency and frequency of urination or explosive defecation The visceral manifestations of the autonomic imbalance often suggest that some acute circulatory accident or shock producing phenomenon has occurred

Reactions to Reality Situations—In striking contrast to the reaction of the patient to the anxiety producing mechanism is the stoical approach to reality situations When the sufferer from an anxiety neurosis is con

sists throughout the life span of most individuals and is relatively unimportant in the full ledger of the years

The Useful Neurosis—In some individuals the neurosis is of positive importance and may be necessary and useful It is the drive behind many great artists musicians writers physicians surgeons and political figures It was undoubtedly to this that Oliver Wendell Holmes referred when he stated that it was the cranks that make the wheels go round In contrast to the socially useful neuroses are the secondary gains which the neurotic wins at the expense of the rest of the community The woman with an hysterical headache or vomiting attacks receives a great deal more attention than her more integrated sister She may be coddled and protected by her family whereas otherwise she might have to assume additional and onerous duties in relative obscurity The neurosis is useful when it can be exploited to the advantage of the possessor The comedian who poses as a neglected unloved tramp is actually parading his neurosis for lucrative emoluments at the box office whether or not this is his deliberate intent We laugh and joke at references to impotence satyrism nymphomania or homosexuality We observe in the arts the delineation of the neurosis in the paintings choreography and the utterances of the artists In these examples the neurosis furnishes a method of expression and often a livelihood for the afflicted In a less obvious fashion the prosaic neurotic utilizes his neurosis through the mechanisms of *sublimation* and *rationalization* The anxious and insecure individual overcompensates and through excessive diligence and application accomplishes stupendous tasks The patient with an obsession or a compulsion becomes a slave to a routine to which he adheres come what may In other instances the drive is sublimated The tippler becomes a reformer the woman of easy virtue a prude and the prevaricator the watchdog of veracity

The Clinical Neurosis—In a relatively small number of individuals the neurosis is neither latent nor useful It interferes with life liberty and the pursuit of happiness It impinges upon the domain of clinical medicine and requires treatment The remainder of this chapter will deal with the clinical neuroses

CLINICAL VARIETIES OF NEUROSES

Before the clarification by Freud of the mechanisms of the neuroses certain descriptive disturbances were recognized and named though the labeling accomplished little purpose other than classification In light of newer developments it becomes apparent that certain of these categories deserve preservation since they afford diagnostic prognostic and therapeutic implications of considerable value

For present purposes the neuroses will be listed in the following manner

- Anxiety neuroses
- Neurasthenia
- Hypochondria
- Conversion hysteria
- Anxiety hysteria
- Traumatic neuroses
- Compensation neuroses
- Compulsion neuroses
- Perversions
- Mixed neuroses

reading and the differentiation reverts back to clinical judgment and a therapeutic test with iodine (p 1218)

If there is the slightest doubt concerning the integrity of the circulatory system the most elaborate laboratory examinations are indicated for the mutual protection of patient and physician An electrocardiogram may reveal surprising changes in either direction When there is reasonable doubt and a probability that organic circulatory disease is present or is accompanying the anxiety it is wiser to suspend judgment and wait upon observation for several hours or even days

Course —The anxiety neurosis may be wholly latent It may be provoked on occasions by all manner of nonspecific stimuli such as trauma illness war deprivation the death of a relative or friend pregnancy the *menopause a fire or an accident* The course may be more or less chronic with such persistent anxiety as to exhaust the good will patience and affection of all members of the immediate family household or social group Anxiety also may be an early symptom of the major psychoses and in the face of doubt observation by a psychiatrist is advisable

Treatment —Many anxiety neuroses are sufficiently mild so that intelligent supportive treatment by the practitioner makes it possible for the patient to live with his neurosis In any event nontechnical psychotherapy is valuable as a therapeutic test with referral to the specialist if there is not a material reduction in the symptomatic difficulties within a reasonable period of time

Reassurance —The elements which enter into a psychotherapeutic result are many and varied The most potent factor is that of reassurance after the completion of the diagnostic survey with particular focus on the area indicated by the symptoms Reassurance is accompanied by the positive assertion that the practitioner regards the complaint as genuine and not as an imaginary figment or an exaggeration The wise physician will stress this point he will not deny the existence of the symptom jeer at it or indicate that the patient is overstating the degree of discomfort Often it is a great comfort to the patient to have the practitioner report that he himself has suffered from the same complaint and testify to the intensity of the distress

Prognosis —Reassurance is fortified by the promise that the symptoms will abate and the prediction that they will recur on provocation If the latter precaution is not taken the confidence of the patient in his therapist may be rudely shattered upon exacerbation of the derangement

Observation of Acute Episodes —The first interview relative to the condition is terminated by the request that the physician be notified in the event of an acute episode Particularly in panic states the patient may accept the fact that he is normal at the time of the examination but will insist that something quite different must transpire during the acute phase such as the *pavor nocturnus* The physician extracts the promise that the patient will hasten to the office immediately the symptoms are noted so that an examination may be made *in the midst of the occurrence*

Follow up Visits —No matter how greatly the patient seems relieved after the first interview a series of follow up visits is planned If the patient seems unwilling to come for an interview it is justifiable to give a hypodermic injection of any bland substance such as neurophosphate a

fronted with a truly serious emergency such as an operative procedure he may respond with courage and steadfastness which amazes the practitioner who has anticipated all manner of annoying and disturbing psychic and emotional overplay

Simple and Complicated Anxiety Neuroses—The anxiety neurosis exists in a *simple* form when it is *unaccompanied by organic disease* An important problem in differential diagnosis arises when the anxiety accompanies a *definitive physical finding,* such as a hypertension, valvulitis glycosuria or albuminuria Under these circumstances it is the function of the practitioner to evaluate the proportion of the distress resulting from the organic finding and that which is derived from the aura of anxiety

Still more difficulty arises when the patient with a known anxiety neurosis develops *acute symptoms* such as pain in the abdomen The practitioner who knows his patient well discounts a certain proportion of the reported complaint as a manifestation of the anxiety neurosis In the back of his mind however he must remember that the patient with the neurosis as well as the normal integrated individual may develop acute appendicitis incarceration of a hernia or perforation of a peptic ulcer There is probably no greater dilemma in the practice of medicine than that of attempting rightly to assign the significance of the symptoms in a case of anxiety neurosis On the one hand the conscientious physician fears to give the symptoms the weight proportionate to the degree of complaint for under these circumstances unnecessary operative procedures may be initiated Opposed to this if the symptomatology is underrated the patient with the anxiety neurosis cries wolf and an inflamed appendix goes onto perforation merely because the overcautious physician has refused to accept the reported symptoms at face value

Pathogenesis of Anxiety Neurosis—The anxiety neurosis is seen throughout life but is most frequent in relatively young patients often of adolescent age The mechanism according to the Freudians is a conflict that is usually related to a healthy sexual appetite without the means for gratification Oftentimes as the analytic school has particularly pointed out the anxiety is in reality the expression of wish or an unsuccessful effort at the attainment of a purpose

Diagnosis—The diagnosis of the anxiety neurosis is made on clinical grounds its positive affirmation does not preclude the possibility of the presence of concomitant organic disease No matter how obvious may be the psychogenic nature of the disturbance both for diagnostic and therapeutic purposes the practitioner is under obligation to perform a *meticulous physical examination* with particular reference to the area organ or tissue to which the symptom is referred The fact that the patient has a neurosis does not eliminate the possibility that he also has a cancer or tuberculosis In the acute panic states the problem is of serious complexity particularly if the symptoms are referred to the circulatory apparatus since the anxiety in and of itself may produce tachycardia elevation of blood pressure and symptoms suggesting peripheral vascular failure (shock)

In the chronic anxiety states there is often a resemblance to *hyperthyroidism* If possible a basal metabolic estimation is performed but often by the very nature of the neurosis it is difficult to get an accurate

thenic may develop superimposed chronic disease such as active tuberculosis carcinomatosis or a blood dyscrasia

Many of the bitterest experiences of clinical practice arise from dealings with neurasthenics Tiring of their old physician they seek a new face or an institutional work up and report in triumph that there has been found a new physical sign such as low blood pressure a fallen womb or a ptosed kidney which explains the symptoms previously dismissed as neurotic With facile ignorance of the total situation the new physician gives symptomatic therapy or performs an operative procedure such as a gynecologic plastic a nephropexy or an appendicectomy For a while a miracle is reported primarily due to bed rest but with recurrence of symptoms the situation is intensified The passage of time reveals the error to the patient but does not repair the injury to the reputation of the original medical advisor

Pathogenesis—Freud s original explanation of neurasthenia was that of an organic neurosis which he attributed to actual debility resulting from excessive sexual activity Later analytic interpretations linked it closer to the mechanisms of the schizophrenic process

The neurasthenic often has suffered from lack of affection and frustration in early life As a child he was unloved unwanted unattractive and unpopular Prolonged and frequent masturbation may represent a compensation for the inattentiveness of others and the inadequacies of parental love

Course—The symptoms of neurasthenia do not usually become manifest until adult life at which time they are precipitated by some life situation such as a disappointment in love or work The younger neurasthenics are almost all early schizophrenics The symptoms are more or less chronic and acute episodes such as characterize the anxiety states are rare

Diagnosis—Since many chronic diseases begin with fatigability and the symptoms of neurasthenia the practitioner refrains from making the diagnosis of the neurosis by any method other than by *exclusion* Early tuberculosis hyperthyroidism diabetes mellitus the blood dyscrasias brucellosis deep seated malignancy the anemias the avitaminoses and adrenal cortical deficiency may begin with identical symptoms The patient is entitled to a complete blood examination urinanalysis the recording of a temperature graph a chest film an estimation of the basal metabolic rate a tuberculin skin test and repeated physical examinations before a definite commitment is enunciated

Since cachexias and chronic infections may arise in the neurasthenic just as in the integrated individual physical examination is repeated at intervals to ascertain that organic complications have not been obscured by the psychogenic manifestations

Treatment—The treatment of neurasthenia is conducted according to the principles of therapy used in the anxiety neurosis (p 1347) Additionally attempts are made to stimulate mind and body

After the patient is assured as to his organic integrity he is told of the presence of positive physical findings such as a low blood pressure a subnormal temperature or a slight anemia Women are made aware of nephroptosis or such gynecological abnormalities as uterine malpositions It is carefully explained that none of these deviations from the normal is

vitamin preparation or distilled water The injection visits give the physician an opportunity to renew his psychotherapeutic attempts The patient often begins to unburden himself of his problems and accomplishes a healthy ventilation The material uncovered affords an opportunity to the practitioner to make interpretations and explanations of difficulties and perhaps link them with the symptoms

At each visit it is wise to reexamine the organ or tissue to which the symptom is referred so that further reassurance is given Meanwhile in a seemingly offhand manner it is often possible to direct the play hobbies recreation studies and reading and the adjustments of the patient to his associates family and environment

As soon as the patient develops an understanding of his difficulties and the anxieties abate the hypodermic injections are terminated but the patient is not discharged He is instructed to attempt to get along on his own momentum but the promise is exacted that upon a return of the symptoms he will resume therapy

Drug Therapy —Psychotherapy is abetted by the use of a *simple sedative* such as phenobarbital 0 015 gm (¼ grain) after meals and a *hypnotic* in average doses at bedtime

Reference to Specialist —The patient with resistant symptoms or prepsychotic manifestations is referred to the psychiatrist for more complete study and observation Provided there is no total personality defect psychoanalysis gives promise of brilliant therapeutic result in obstinate anxieties for more rapid results the hypnagogic reverie (p 1328) may be tried

NEURASTHENIA

The symptom complex of neurasthenia is characterized by excessive mental and physical fatigability irascibility a tendency to depression cardiac irritability headache sexual difficulties and gastro intestinal symptoms In general the neurasthenic is a discouraged and disappointed person Little pleases him and nothing is truly satisfying His sexual life is especially annoying for either the libido is lacking or potency is impaired The female is usually frigid or at best lacking in normal sexual response Almost invariably in neurasthenia there is a problem of masturbation This habit has usually persisted into adult life and is associated with considerable shame and a feeling of guilt In fact the feelings of weakness and irritability are usually attributed to masturbation

Examination of the neurasthenic often reveals a subnormal temperature a low blood pressure a slow pulse rate and a lowering of the basal metabolic rate without clinical evidences of hypothyroidism

Simple and Complicated Neurasthenia —In *simple* neurasthenia there is no insurmountable difficulty in eliminating the possible presence of organic disease *Complicated* neurasthenia is that in which there is a superimposed and unrelated pathologic change or in which organic disease develops in the patient who previously suffered from simple neurasthenia

As in the anxiety neurosis the practitioner must guard against diagnostic pitfalls He is called upon to evaluate the symptomatology in the neurasthenic who has also a healed tuberculosis at an apex a mild anemia a persistent hypotension some albuminuria or glycosuria His knowledge of his patient s neurosis must not obscure the possibility that the neuras

assistance of massage graded exercise and water cures occasionally achieves results that cannot be obtained at home See p 3764

Formal Psychotherapy—Formal psychotherapy is most disappointing in the treatment of neurasthenia Unless attempted early in the course of the process even an adequately performed psychoanalysis has no brilliant prospect of success Shock treatment may be tried in desperation with little promise of more than passing benefit

Hypochondriasis

Hypochondriasis is probably not a separate neurosis but is more likely *a neurotic symptom encountered in the setting of almost any other neurosis* It consists of an exaggerated preoccupation with the body and its functions It may or may not be associated with fear and anxiety To the hypochondriac each deviation in function and feeling assumes the proportion and significance of a major illness until the neurosis occupies the main interest and concern of the patient s total energy

Pathogenesis—The hypochondriacal patient is consumed with an interest in his own body (*narcissism*) and apparently enjoys the punishment of the emotions set up by the hypochondriacal response (*masochism*) *The neurosis is associated with insecurity and a feeling of rejection* In a sense the preoccupation with one s own body represents *an attempted compensation for the lack of interest by others*

Diagnosis—The hypochondriac is entitled to a consultation with the specialist psychiatrist since the symptoms may be the early manifestations of *schizophrenia* or the depressed stage of a *manic depressive psychosis*

Treatment—An attempt may be made by the practitioner to treat hypochondriasis in the manner of neurasthenia (p 1350) After a reasonable effort and almost inevitable discouragement the patient is encouraged to apply for formal psychoanalytical therapy since less drastic measures offer little hope of a satisfactory result Shock treatment may be attempted as a measure of desperation in a probatory fashion

Conversion or Transference Neuroses (Hysteria)

The Freudian concept of hysteria involves conflict between personality *and a wish that is out of harmony with the ego and is repressed* The repression is unsuccessful and the unconscious wish being dynamic forces its way into consciousness in a disguised symbolic form The resultant hysterical symptom is thus a compromise

The term conversion hysteria coined by Freud designates the phenomenon whereby emotional conflicts are referred to or projected as bodily symptoms An anxiety hysteria exists when the conversion mechanism has an additional component of fear

The Hysterical Personality—The hysterical personality makes the impression of an immature individual Emotional affects are free easily stimulated and histrionic although psychosexual development may be full and complete The hysteric is usually shy and reserved but given to intense demonstrativeness There is an obvious contrast between the shal

the cause or the result of the neurosis If this precaution is not taken the next examiner may seize on the tangible evidence as a 'pathogenetic straw with a resultant exploitation of the patient and condemnation of the better informed physician It would be impossible to estimate the number of unnecessary operative procedures, particularly in the field of gynecology, that have been performed for the relief of symptoms due to neurasthenia The temporary benefits of these adventures into surgery are the delight of those who report short term results but they are the despair of the compleat practitioner' to whom the patient eventually returns with all of the pristine disturbances

The neurasthenic is stimulated to more intense effort at work play hobbies or recreations It may be possible to remotivate efforts and sublimate them in some useful direction Often a neglected neurasthenic responds with almost pathetic eagerness to the normal amount of interest and kindliness

Drug Therapy—Repeated visits are assured by the administration of some type of hypodermic injection One of the commonest forms of injection therapy consists of the use of the so called neurasthenic serum" which is nothing other than glycerophosphates with a modicum of cacodylate of soda Enthusiasts for vitamin and hormone therapy give mixtures of the soluble components of B complex or adrenal cortical substance The latter is particularly indicated by the resemblance of some of the symptoms of neurasthenia to Addison s disease A simpler and less expensive approach to the same end is accomplished by advising the ingestion of sodium chloride in daily doses of 3 to 6 gm Unless the patient or his physician notes a seemingly specific improvement from hypodermic injections this form of therapy is discontinued as soon as possible

The hypodermic injections are then supplemented by the oral administration of *amphetamine sulfate* (benzedrine) using 2 5 or 5 mg ($\frac{1}{24}$ to $\frac{1}{12}$ gr) each morning on arising and again at noon time provided that nocturnal sleep is not disturbed While benzedrine is being administered a *hypnotic* (*q v*) is ordered at bedtime to assure adequate sleep

The patient with a low basal metabolic rate receives corrective doses of *thyroid extract* (p 1189) When the level of oxygen consumption approaches the normal the physician decides on the basis of the patient s subjective response whether substitution therapy should or should not be continued In the event of reasonable doubt the drug is stopped for a trial period of three weeks in order to obtain more conclusive information

Each form of drug therapy has advocates and occasional success By and large the lack of consistency and the numbers of the specifics lead to the inescapable suspicion that the common denominator for good is the faith of the patient and the suggestion that is practiced purposefully or subconsciously by the therapist Under no circumstance is a permanent result anticipated and the patient often must resolve to endure the symptoms and live within the limit of his capacities

Rest Cures—At times the practitioner despairing of other forms of therapy attempts a *Weir Mitchell rest cure* often with surprisingly good results Naturally the effects are not permanent and upon discharge the patient is warned that a recurrence is to be anticipated under which circumstance the rest cure is repeated *Spa therapy* with the adjuvant

whereas in anxiety hysteria the anxiety breaks through Similarly in a *hysterical depression* the depression breaks through the symptomatic expression or the patient alternates between the neurotic mood and the conversion process In true conversion hysteria the patient is indifferent to his illness whereas in the mood disturbance there is suffering and a desire for treatment

The patient who develops anxiety hysteria is usually immature and suffers a great mistrust of other people There may be a surface friendliness but it is a veneer that does not stand the test of conflict Often the anxiety hysteric has been a spoiled child of unreliable and undependable parents who has been given excessive adoration in brief moments and long periods of neglect Usually material gifts have been offered instead of continued emotional security As a result these children suffer from rages and tantrums They enjoy an extravagant fantasy life along romantic and erotic lines This is often reflected in their dress which is gaudy with an excessive use of cosmetics and an assumption of seductive behavior The outward appearance usually cloaks a lack of experience or actual frigidity

Pathogenesis—Conversion hysteria is a reaction adopted unconsciously for a very definite purpose It serves to disguise some problem frequently the satisfaction of a wish whose conscious gratification cannot be permitted The conflict that arises is converted from an emotional difficulty into a bodily symptom Thus the Freudian explanation reveals the purposefulness of the symptom despite the fact that the patient is consciously unaware of its function It explains the unconscious gratification that the patient derives from his symptom and the marked contrast which exists between the seeming shallowness of the emotions and the intensity and dramatic manner in which they are expressed

Diagnosis—The possibility of conversion hysteria is the lurking figure that haunts every diagnostic problem The astute practitioner can only avoid serious difficulties by positive exclusion of every other possibility Nor should he fall into the error of interpreting as hysterical every disturbance occurring in a hysterical individual The sufferer from hysteria is as apt to develop acute appendicitis organic cardiac disease tuberculosis or carcinoma as his emotionally normal fellow

In his dealings with the hysterical personality the practitioner should maintain a high index of suspicion relative to conversion symptoms but he should not take the step between suspicion and definitive diagnostic commitment until he has exhausted all physical and laboratory methods of investigation Consultants are used freely especially when there is the possibility of a surgical condition

Treatment—Since the manifestations of hysteria are characterized by sudden onset and sudden dissipation treatment by almost any means is capable of apparent success Hysterical patients are the prize of all charlatans and fakirs within and without the medical profession They are relieved of their symptoms by suggestion faith hypnosis religion yoga massage glands vitamins hypodermic injections electrotherapy the actual cautery pink pills bizarre diets incantations Voodooism and modalities of similar ilk

The suggestibility of the patient arouses a state of alertness in the conscientious practitioner He recognizes that almost any element in

lowness of the emotions and the intensity and theatrical effects with which they are expressed The patient in an hysterical outburst, simulates the actor whose burst of passion turns off like a light when the curtain of the drama descends It soon becomes apparent that emotions are mostly spurious and feigned

The hysterical personality is usually capable of only brief personal attachments More normal individuals tire of the drama that has repetitiveness and intermissions but no final curtain

Clinical Manifestations of Conversion Hysteria—Conversion hysteria is the least severe and the most easily curable of the neuroses The conflict usually appears at a later period of childhood The symptoms arise suddenly and dramatically and often leave in similar fashion Actually however the underlying tendency to conversion is quite as obstinate as any other basic neurotic mechanism with the consequence that on provocation the patient is likely to flare up with other conversion symptoms

The variety of the conversion symptoms have been previously noted (p 1341) They run the entire gamut of the subjective complaints and objective manifestations known to clinical medicine They include sensory motor autonomic visceral psychic and emotional manifestations

The *sensory complaints* include pains such as headache coccygodynia mastodynia and glossodynia paresthesias may be pruritic particularly in erogenous zones such as the vulva vagina rectum and anus and there may be anesthesia hemianesthesia anosmia amaurosis *myopia mutism* and the like *Motor abnormalities* take the form of spasms or palsies The repertoire includes tics tremors contractures palsies stammering stuttering and aphonia

The *autonomic manifestations* may be vasodermal cutaneous or referable to the functional disturbances in the structures containing smooth muscles There are thus produced gastric and intestinal neuroses globus hystericus aerophagia cardiospasm anorexia nervosa bulimia pica nervous vomiting attacks of diarrhea or obstinate constipation vaginismus peroneal spasm urinary retention instability of pulse rate and rhythm hypertension hypotension lability of the blood pressure episodes of tachycardia and cardiac irregularity peripheral vascular spasms sighing and gasping respirations bronchospasm and the like With severe autonomic imbalance or protracted smooth muscle and glandular disturbances *somatization* results and organic disease is produced as an end result of the conversion hysteria The complete list of the *psychosomatic manifestations* is elsewhere given (p 1344) but the commoner syndromes include peptic ulcer essential hypertension and neurodermatitis

Finally the hysterical individual may develop *psychic* and *emotional* disturbances which simulate the psychoses They may involve perception (p 1292) consciousness (p 1293), attention (p 1296), thought production *content and progression (p 1297) memory* (p 1298) affect (p 1300) appetite (p 1302) sexual behavior (p 1298) sexual function (p 1304) sleep (p 1304) motor behavior (p 1308) speech (p 1310) and posture (p 1310)

Clinical Manifestations of Anxiety Hysteria—An anxiety hysteria is merely a conversion hysteria with an additional symptomatic anxiety In the true conversion hysteria the patient has masked completely all affects

COMPENSATION NEUROSES

There is a high incidence of neuroses which follow trifling accident or injuries when the patient receives compensation from an insurance company or from the state The symptoms include the entire battery of neurotic difficulties anxiety states and symptoms simulating conversion hysteria The conditions have in common a striking disparity between the minimal injury and the maximal amount of emotional involvement The differentiation of a traumatic neurosis from malingering may tax the skill of the specialist to whom the problem is referred particularly in view of the litigious possibilities

Perhaps the most important aspect of these conditions is the basic postulate that no traumatic neurosis can be successfully treated as long as the patient is receiving compensation It is vastly to the patient s ad vantage that he receive a lump settlement pay for his own therapy and make his adjustment within the framework of his compensation

NEUROSES OF REGRESSION AND PERVERSION

The neuroses of regression and perversion represent fixations at in fantile levels They are difficult of treatment but fortunately much less common than the simple and conversion neuroses

Clinical Manifestations of the Compulsion Neuroses —Compulsive acts of significant degree are fortunately uncommon They represent an intrusive need to act or think in a definite repetitive manner despite the intellec tual awareness of the uselessness of the act or thought of its disagreeable or painful nature The patient is compelled to think or act in a particular manner despite reason will power determination or a sense of humor

Many patients have routines of behavior to which they cling tena ciously and without which they feel uncomfortable They have certain rituals in arranging clothes pillows and chairs They must go to bed make love attend to their bodily needs conduct their businesses and manage their households in a set fashion despite the inroads that their conduct makes upon their own or their associate s comfort convenience and econ omy Occasionally the compulsive idea takes on the nature of a religious ceremonial or a superstition such as touching wood stepping on the cracks in the pavement or avoiding the cracks in the pavement At times it becomes necessary to count numbers count windows the number of steps or the number of cars in a train The obsession may be relative to health and require repeated washing of the hands violent daily catharsis repeti tion of enemas and colon irrigations or an aversion to shaking hands be cause of fear of soiling and contamination There may be doubts concern ing the locking of a door the closing of a window or the turning out of the lights and gas jets Much more serious are the compulsions relative to jumping off a height plunging a knife into flesh or the impulse to dive under approaching trains

In addition to these compulsive acts are compulsions in thinking in which the train of thought cannot be interrupted and must proceed along certain lines (*idee fixe*) The compulsion or obsession may take on anti social manifestations such as kleptomania pyromania dipsomania toxico mania or trichotillomania

which the patient has faith will produce relief of symptoms and he does not wish to be misled by his apparent therapeutic triumph He knows that the symptoms will recur on provocation and that the patient who elaborately sang his praises and flattered his ego as of the current week may with equal fervor and enthusiasm brand him as an ignoramus and fakir and start a campaign to have his license taken away before the sun sets on another day

Conscious of the volatility of his patient the practitioner proceeds with caution and timidity He reassures his hysterical patient that there is no evidence of organic disease and follows the principles laid down in the management of the anxiety neurosis (p 1347) He exerts even greater care to avoid any implication that the disease is imaginary the symptoms exaggerated or the condition hysterical After several sessions for which the patient returns for hypodermic injection or the application of some physical modality the psychotherapeutic approaches assume increasing prominence and the tangible modalities are dropped *Sedatives* and *hypnotics* often assist in the progress of events When the confidence of the patient has been obtained and the symptoms begin to abate or entirely disappear the superficial conflicts become apparent through the patient s free ventilation

As soon as the symptoms lessen it is wise to warn of *recurrences* and *exacerbations* on provocation and then is the time to intimate that there is a relationship between psychic conflict and clinical disturbance The patient being more or less educated to this thought through the course of previous conversations resents the implication less acutely and may even leap at the explanation In more favorable instances adjustments remotivations and sublimations may terminate the problem

The patient who has refractory manifestations recurrences or possible psychotic personality difficulties is referred to the trained psychiatrist Again almost any type of psychotherapy will yield a favorable result but the more permanent and complete effects are to be anticipated from the psychoanalytic approach Shock therapy is ill advised but hypnosis and the hypnagogic reverie are worthy of trial under expert supervision

TRAUMATIC NEUROSES

The traumatic neuroses are usually included in the group of hysterical disorders They usually occur after events in civil or military life which are interpreted by the individual as a sudden threat to his existence Kardiner has postulated that the traumatic neurosis develops as a protection against further hurt from a hostile world The patient looks upon himself as helpless in this world and may revert to childlike mechanisms in the service of this need for defense

The milder manifestations include irritability excessive sweating trembling dizzy spells tics nausea and vomiting There may be confusional states fugues and isolated conversion phenomena Quite characteristic of the traumatic neuroses are terrifying dreams which repeat the provocative experience

The *treatment* of traumatic neurosis is best left to the specialist who requires an extraordinary degree of skill and much experience

serious psychoses and this decision is *specialist* province The differential diagnosis of neurosis versus psychosis is elsewhere delineated (p 1318)

Treatment—The treatment of compulsion states and perversions is difficult and unrewarding A *psychoanalytic* approach may be of considerable value if the condition is not of excessively long duration so that the entire personality has become involved in a rigid obsessional pattern

Shock therapy has been used with some degree of success but is not employed unless the incapacity justifies the risks of the procedure Examples of conditions which warrant shock therapy are the manias which have legal implications such as kleptomania pyromania or compulsive exhibitionism and the perversions In desperation prefrontal lobotomy may be attempted

Mixed Neuroses

It is unusual for any neurosis to conform strictly to any of the patterns previously described Even the well integrated physician recognize that he himself reflects anxieties fears compulsions obsessions and mild conversions He knows too that normal sex life is associated with occasional furtive dallyings with the mechanisms of perversion The neurotic also presents a galaxy of clinical phenomena Rarely do these reaction pictures fit into any definitive pattern and in a sense all neuroses are mixed The exact classification which has some prognostic and therapeutic implications rests upon the dominant presenting derangement

DISORDERS OF TOTAL PERSONALITY

The disorders of total personality include the *abnormal conduct and behavior patterns* as well as the *psychoses* These in contrast to the partial reaction of the neurosis are total personality disturbances The minor manifestations are the province of the practitioner but the management of the psychoses enters the province of the specialist often with medico legal implications

Personality Behavior and Conduct Disorders

The individual personality and behavior pattern varies according to many characteristics which include physical qualifications intellectual and educational attainments emotional social moral and spiritual components and hereditary acquired financial ethical and political influences

The practitioner learns to expect more of a husky healthy adult than of a puny sickly child The patient who has had educational advantages ought to be more reasonable and tractable than the illiterate though this is not always in accordance with experience Varying degrees of conduct are anticipated in individuals brought up under varying social circumstances The child reared in the home of the lord of the manor is expected to demonstrate more of the social graces than a field hand whose habitat is the barn though this may not necessarily be the case Moral and spiritual values vary in different communities and in different portions of the same community and each is judged by the surroundings in which he was cultivated

In the majority of instances the compulsions are mere habits and it is doubtful whether any one of us is completely free from at least one manifestation It is when the resistance to the obsessional pattern causes extreme discomfort interferes with daily routine or prevents functioning where it is so bizarre as to be obtrusive and painful that the realm of clinical medicine is entered and symptomatic relief is sought Under these conditions the personality becomes dominated by the neurosis and failure to act in the compulsive manner is associated with severe superimposed anxiety

At times the compulsion is socially useful Under these circumstances the patient is scrupulously neat and orderly almost to a fault Hyperconscientiousness and shyness conservativeness and penuriousness miserliness and general conformance are in a final analysis compulsions While they seem to be social assets actually the individual who exhibits these traits is dependent and requires a good deal of reassurance and approval

Pathogenesis —The seeming lack of meaning and reason in the compulsive acts becomes clarified in the interpretation of the Freudians The original compulsive idea is a psychic phenomenon which has been elaborated as a defense against an early sex transgression The original objectionable idea containing a charged emotional content is repressed the affect is dissociated from the idea and attached to a harmless concept which is then permitted to enter consciousness A further defense against the repetition of the tabooed wish is the development of a ceremonial which is attached to the obsessive idea Though the compulsion seems completely dissociated from reason and the normal mental processes analysis establishes that the compulsive thought or action is actually a useful symbolic defensive mechanism of the unconscious It is necessary to the mental economy and serves as a *compromise gratification of infantile wishes* the obsession substitutes gratification for repressed guilt laden and feared desires

The neurotic uses his rigid attitudes and methods of reaction in an attempt to achieve a feeling of safety and security as though he would create a world so full of order and regulation as to protect himself from the problems and disorders of everyday life To accomplish this in the execution of the compulsion or obsession the individual may face danger humiliation jeering degradation and bodily injury

Clinical Manifestations of Perversion —The various deviations of sexuality, sexual behavior and sexual intercourse are elsewhere described They may serve in normal individuals as variations on a theme or as prologues or accompaniments to fornication in the natural manner When they dominate sexuality to the exclusion of normal relationships they enter the realm of the neuroses of regression and present profound clinical problems often complicated by disturbances due to shame guilt hostility, alcoholism and addiction

The perversions (p 2409) are franker fixations of infantile sexual development and are very resistant to treatment

Diagnosis —The diagnosis of compulsional neuroses and the perversions offers no difficulty relative to somatic medicine It is important however to ascertain that the manifestations are not herald symptoms of the more

Manifestations of Conduct Disorders —The conduct disorders created by personality difficulties and the psychopathic personality are legion They begin in childhood and end with senility They include crying spells tantrums by day and terror dreams by night failure to accomplish control of the urinary and defecation reflexes fears abnormal obstinacy lying cruelty *spitting up and vomiting of food day dreaming* lack of sociability truancy nail biting thumb sucking stammering stuttering insomnia cyclic vomiting anxiety phobias obsessions compulsions tics manifestations of hysteria dulness backwardness *maladjustments in social groups* and contacts misconduct in school overzealousness in conduct behavior and studies masturbation enuresis food capriciousness destructiveness sleep-walking conflict with fellow pupils or teachers and abnormal shyness

Adolescent personality problems include excessive emotional reactions relative to adventure and exploration worry egocentricity disturbance in sexuality such as excessive masturbation inordinate interest in the opposite sex inordinate shyness and retreat from the opposite sex crushes for individuals of the same sex running away from home or inadequate emancipation from parents and the household juvenile delinquency feelings of inferiority or superiority and the tragedy of adolescent suicide

In adult life the problems that are commonly encountered include lack of success or inordinate preoccupation with the career profession or business failure to marry or the accomplishment of a bad marriage sexual maladjustment in marriage either excessive insufficient or uncoordinated intercourse tendencies toward homosexuality and perversion child parent and parent child misunderstandings and maladjustments and parsimony and lavishness

Problems of the *aged* are most tragic The gaffer and his granny deteriorate interest in others is lost egocentricity is emphasized neatness and decency are replaced by untidiness soiling drooling and sexual exhibitionism by word and deed

Complications —The psychopathic personality tends to get into difficulties with all manner of antisocial conduct Criminal personalities delinquents vagrants prostitutes zealots hermits religious maniacs reformers *moralists super athletes* sex perverts *drug addicts* and *suicides* are recruited from within their ranks

Sexual Perversion —See p 2409

Drug Addiction —The common types of drug addiction include alcoholism morphinism cocainism the inordinate use of bromides barbiturates and hypnotics and the smoking of marihuana

Independent of the type of addiction the problem is essentially that of dealing with a personality deviation With relatively few exceptions the addict is a distorted personality It is the normal reaction to use *drugs when needed and to eschew them as soon as the indicated symptom* has abated It is for this reason that we have elsewhere stressed the psychological rather than the pharmacological approach to the treatment of *alcoholism* (p 3818) *morphine addiction* (p 3861) *cocainism* (p 3916) and habituation to sedatives and hynotics (p 3843) The marihuana problem is beyond the province of medicine since it constitutes a legal *offense and is to be handled by the proper authorities*

The assessment of standards is certainly not the business or the province of the practitioner However when dislocations occur which give rise to clinical symptomatology or interfere with the welfare security and peace of the patient and his environment, the problem is often deposited in the lap of the family doctor

Types of Disturbed and Psychopathic Personality —Deviations of personality are of great importance from the viewpoint of the individual and of society Patients may present a host of varying difficulties manifestations and symptoms These may be transitory or episodic or they may be chronic and persistent They may be accepted as manifestations of 'queerness" or 'eccentricity' under which circumstance they have mere nuisance value' or they may reach the point where they disturb the pursuit of a human life and harass household social and business associates

In general the personality disorders are characterized by *emotional insecurity* and *childishness* The patient is often unreliable and irresponsible Difficulties begin in childhood and continue with or without interruption throughout school years and the span of a life There seems to be no capacity to learn from experience Impulsive behavior without regard to the welfare and needs of others characterizes conduct Underneath a surface cleverness and glibness there is often bad judgment and a total lack of regard for truth and honesty

In the *neurotic behavior disorder* the neurotic mechanisms manifest themselves in disturbances in the mode of living with relatively few outspoken neurotic symptoms The *psychopathic behavior disorders* represent personality disturbances in which psychotic mechanisms disturb the general adjustment to life without the production of a fullblown psychosis The psychotic personality will cheat badger and steal without a sense of shame He frequently involves others in manipulations often with tragic consequences to innocent members of a family or their friends The psychopaths are notorious liars and purveyors of wild unreal schemes always with totally unwarranted expectations of success

Throughout these excesses these patients exhibit a poverty of assets They are incapable of lasting adult love relationships Their companions most often are like themselves in that they are selfish inadequate irresponsible and impulsive—all of which may be summarized by the terms *egocentric* and *narcissistic*

As *complications* of the psychopathic personality there result excesses in drinking in the use of tobacco and drugs sexual perversions and criminality Bad marriages and divorce mark and suicide frequently terminates their earthly careers Their roster includes perverts criminals tramps crackpots unsuccessful inventors and visionaries pathological liars eccentrics hoboes hermits and seekers after glory At times the psychopathic personality makes a virtue of his shortcoming and succeeds as an artist a religious or political reformer or as a leader of the rag tag and bobtail

Etiology —The etiology of personality disorders is not clearly defined The factors of heredity alcoholism poverty malnutrition and illegitimacy have been stressed As usual the organicists have sought the answer in pathologic changes such as might occur with inflammation particularly congenital syphilis but the evidence is meagre and unconv

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While it is true that the practitioner rarely has expert knowledge of many of the personality disorders and their ramifications there is often no one else to whom the *disturbed family* group can go *Under* these circumstances there is no alternative but to make a determined and honest effort to accomplish a solution that promises the greatest prospect of benefit for the greatest number

Suicide —There has been an alarming increase in the incidence of self destruction The physician is required to protect his patient and himself by meticulous efforts at prophylaxis and by his refusal to fall into the commission of many common errors for which atonement is difficult Thus it is not true that (*1*) patients who threaten suicide will never make the attempt (*2*) the patient who has attempted suicide by one method is restricted to that device and if protected from this particular type of hara kiri is safe (*3*) the emotionally disturbed patient in a stage of recovery is safe from suicidal tendencies and need not be so carefully watched and (*4*) suicide is prevented by appeals to reason morality and fear of the hereafter

In his dealings with potential suicides the physician strives to make all of his mistakes on the side of conservatism It is his function to protect his patient and himself by demanding twenty four hour professional nursing care or removal to an institution Under any other circumstance he is wise if he disclaims responsibility and refuses to participate in the handling of the situation unless fortified by specialist consultation with explicit direction

Partial Suicide — Partial suicide is attempted by the demand of the patient for multiple surgical procedures The tonsils and adenoids are removed, the appendix and gallbladder are sacrificed the female genitalia are removed piecemeal or at one swoop In each instance the indications seem questionable and the surgical failure is described with a curious mixture of pride and dismay The astute practitioner is wary of the veteran of many surgical amphitheatres particularly if there are evidences of personality and conduct disorders In the presence of at least one relative the practitioner counsels reference to a trained psychiatrist

Management of Personality Disorders —The practitioner successfully deals with most conduct disorders though there is no method by which he may alter the personality pattern In general his management consists in an exploration of the troublesome situation correction of misinformation and in reeducation and adjustment of the involved individual

Exploration of the disturbing situation often reveals that the accused individual is not alone at fault More often than not particularly in childhood disturbance the disorder rests with misdirected zeal a neurotic tendency or misinformation on the part of the parents Crying spells and terror dreams with bed wetting often result from horror stories in the fairy tales or heard on the radio Lying and stealing are devices used to escape inordinately severe punishment for minor acts of naughtiness The child of a matriarch may respond by complete loss of initiative or an arrogant hostility

Many of the adolescent difficulties and maladjustments of adult life stem from the large mass of *absolutely authentic (mis) information* with which each individual is bombarded from all sides The majority of misconceptions deal with sexuality It is a source of recurrent amazement to note how much good can be accomplished by a straightforward explanation of sexual hygiene In households where it seems impossible to accomplish a satisfactory adjustment it may be necessary to send a child to boarding school or a summer camp The aged are often happier and better cared for in institutions devoted to their problems

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CHAPTER 65

PSYCHIATRY THE PSYCHOSES

THE psychoses are disorders of total personality Their differentiation from the neuroses has been given previous consideration (Table 86 p 1313) The psychoses are subdivided arbitrarily into idiopathic and symptomatic varieties

SCHIZOPHRENIA (DEMENTIA PRAECOX)

The schizophrenic reaction is a psychotic disturbance characterized by a cleavage or splitting between ideational contents and affect Closer to the core of the schizophrenic process however is the disturbance in the accurate relationship to external reality Since the disturbance is encountered most often in the 'teen age groups and the early twenties it has also come to be known as dementia praecox or the nervous breakdown of the young

Schizophrenic reactions constitute a grave and frequent type of mental disease It is estimated that 40 000 patients annually develop dementia praecox in the United States The vast majority of these require institutionalization and since the course is usually progressive without striking therapeutic benefits the span of occupancy averages one to two decades to the detriment of all concerned

The Schizoid Personality —Schizophrenic reactions usually but not invariably develop in individuals of the so called schizoid personality Since the manifestations of the latter are usually first observed by the practitioner at a time when treatment offers the best possibility for benefit it is important to stress these traits as harbingers of later danger

Alarming personality traits which arouse suspicion include the *brooding post adolescent* for whom no one is good enough and whom nothing pleases the *antisocial person* who is overcritical of everyone and everything, who finds satisfaction only in himself and in his fantasy life and

who hides behind superior attitudes the *persistent masturbator* especially the one who is worried about his habit fights unsuccessfully to control it and has great feelings of guilt relative to it the *intense bookworm* who is so preoccupied with philosophic speculations and the quest for the absolute that he misses the direct satisfaction obtained from relatively simple outlets such as interpersonal relationship the *overreligious* especially those preoccupied with mystical elements and religion and those who personalize experiences the *stubborn unpersuadable person* who is indifferent to the emotional needs of others and is given to frequent displays of temper the *odd individual* whose behavior is marked by strange quirks who is unsocial and seemingly oblivious to the ordinary demands of the community the *tense shut in* who can open up to no one and who is unable to share painful situations or entrust difficult decisions to those whom he seemingly loves and trusts

TABLE 87 —DIFFERENTIATION OF IDIOPATHIC AND SYMPTOMATIC PSYCHOSES

	Idiopathic Psychosis	Symptomatic Psychosis
History	Of personality disturbances (p 1359)	Of definite trauma infection or intoxication
General physical status	Negative	Positive findings in syphilis and vascular diseases
Neurologic physical examination	Negative	Positive findings particularly in syphilis following encephalitis or meningitis and with neoplasm
Cerebrospinal fluid	Negative	Positive findings in syphilis encephalitis and meningitis
Other laboratory findings	Negative	Positive findings in syphilis metabolic disturbances such as hyperthyroidism and diabetes mellitus renal or hepatic insufficiency and hyperchromic anemia

In brief the practitioner is wary of young people who are acutely out of harmony with themselves their families and their community and for whom the usual adjustments in the art of living have been too painful and too difficult

Clinical Manifestations —The schizophrenic reaction is usually simple paranoid catatonic or hebephrenic

Simple Schizophrenic Reaction —The simple schizophrenic reaction consists of a gradual withdrawal from reality The patient becomes increasingly dull and apathetic he shows no interest in the world at large or in his smaller immediate world and he lacks ambition and initiative Despite apathy and indifference the schizophrenic often becomes irritable and moody for no consistent conscious reason Mental and intellectual deterioration slowly develops Hallucinatory experiences and delusions are rare Neglected individuals who suffer from this reaction sink into prostitution vagrancy and hoboism

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Hebephrenia—The hebephrenic schizophrenic reaction type is the least clearly defined It is characterized by silly behavior grotesque mannerisms incoherence of thought inadequate and seemingly unmotivated emotional responses laughter and crying

Etiology and Pathogenesis—The etiology and pathogenesis of the schizophrenic reaction types remain a mystery The psychoanalytically trained psychiatrists emphasize the role of emotional conflict Others deprecate these factors and stress constitutional hereditary and biological factors If there is a hereditary basis for dementia praecox it is yet to be proved Whereas schizophrenia occurs more frequently in certain families it may arise in the midst of perfectly good inheritance

There is no known pathology of schizophrenia Questionable changes are described in the brain and other organs especially the endocrine glands but these probably are secondary and are characterized by being highly inconsistent

Diagnosis—The diagnosis of schizophrenia depends upon the personality determinants The physical examination reveals no abnormalities and

TABLE 58—RESULTS OF ELECTRIC CONVULSIVE THERAPY IN [illegible] CASES OF SCHIZOPHRENIA

	Total	Recovered and Much Improved	Improved	Unimproved
Less than 6 months	60	41 (68 3 per cent)	13 (21 7 per cent)	6 (10 per cent)
6 months to 2 years	8[illegible]	31 (41.5 per cent)	24 ([illegible]9 3 per cent)	[illegible]4 ([illegible]9 3 per cent)
More than 2 years	87	8 (9 [illegible] per cent)	36 (41 4 per cent)	43 (49 4 per cent)
Old cases with previous remissions	48	[illegible]6 (5[illegible] [illegible] per cent)	10 ([illegible]1 7 per cent)	10 (21 per cent)
Total	275	10[illegible]	[illegible]3	8[illegible]

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there is no assistance other than of a negative quality to be obtained from the laboratory

There should be no difficulty in differentiating schizophrenia from the neuroses since the latter as has been previously related are partial personality disorders (p 1313) The greatest problem arises in determining where the schizoid personality ends and the psychotic schizophrenic reaction begins This qualitative decision is best left to the consulting psychiatrist who in point of fact may require weeks or months of observation before a definite decision is forthcoming

Prognosis—There should be no tendency to underrate the gravity of the prognosis in schizophrenia Nevertheless the recent introduction of the various forms of shock therapy have somewhat relieved the previous outlook of utter hopelessness In general patients who have had a relatively acute onset have a better response to treatment Older patients and those who have had the disease for any length of time deteriorate emotionally and intellectually They run a chronic and subchronic course and form a huge case load in the mental disease hospitals

Paranoia—The paranoid schizophrenic reaction type is characterized by active delusions of a persecutory or grandiose nature with well marked ideas of reference (p 1297) Auditory and visual hallucinations are common (p 1293) The patient's life rapidly becomes disorganized He is quarrelsome and suspicious He gives up work and may refuse to eat because of the fear that the food is being poisoned He may commit acts of violence and destruction in response to hallucinatory experiences Hence the paranoid schizophrenic comes in conflict with law and enters the category of the 'criminally insane

Catatonia—In the catatonic schizophrenic reaction types there are fluctuating episodes of depression excitement and stupor These may be preceded by other schizophrenic manifestations but often are fairly acute

DIFFERENTIAL DIAGNOSIS OF

Idiopathic Psychoses

The differential diagnosis of the idiopathic psychoses is dependent upon clinical features since neither physical nor laboratory findings are pathognomic

VARIETIES	DIAGNOSTIC FEATURES
Schizophrenia	Patients between 13 and 25 years old History of eccentricity in adolescence Manifestations may consist of withdrawal from reality splitting of personality paranoia or catatonia (p 1364)
Manic Depressive Insanity	Usually occurs after 25th year History of swings in mood from gayness to sadness Manifestations may feature phases of expansion or depression with remissions (p 1368)
Involutional Psychoses	After climacteric in females more frequently than in males History of prior maladjustment Manifestations often related to psychosexual inadequacy (p 1372)
Paranoia	Schizoid phenomena in older patients Manifestations usually delusional or persecutory (p 1373)

in their onset In a stuporous phase the patient sits or lies about quite cut off from the world of reality There may be negativism or waxy flexibility (p 1310) in which bizarre positions are maintained without change for hours Lesser degrees of stupor are characterized by great indifference stereotype of action and words (p 1309) echopraxia and echolalia (p 1309) Stuporous patients often hallucinate and have delusions of persecution or grandeur (p 1296)

Extreme excitation may alternate with the stupor Under these conditions the language and behavior are transformed into intense violence and homicide and suicide may occur Hallucinations or delusions are present and the excitation lasts for several days until the stupor again supervenes

may precede a fully developed phase of excitation Contrariwise the hypomanic may develop irritability and a process of slowing down as if suddenly he were compelled to leave a concrete road and continue his course in heavy sand or mud

Phase of Expansion —Evidences of the illness appear characteristically in the spheres of the emotional and mental life the mood stream of thought and psychomotor activity In the *expansive phase* the mood is one of elation supreme self confidence and increasing assertiveness The patient becomes restless and easily distracted The speech at first is voluble and high pitched Later the content has no conscious direction and is determined by the mere sound (*clang association*) There is true flight of thought with a rapid shifting from idea to idea Stimuli pour from within and without and no one idea is fully developed or completed The patient loses all the ordinary self regulation of behavior and becomes obscene and exhibitionalistic with uninhibited eroticism and excessive drinking particularly dipsomania The phase may terminate in a state of delirious mania with extreme violence uncontrollable excitement and a tendency to destruction

Phase of Depression —In the depressed phase the individual seems excessively timid hyperconscientious prudish shy and self deprecatory He is given to worry about petty details especially those having to do with money food cleanliness and toilet hygiene The complaints include easy fatigability a sense of weakness depression the blues headache frequently in the back of the neck gastro-intestinal upsets with loss of appetite distaste for food and bad taste in the mouth restlessness and unsatisfactory sleep in which the patient awakens more exhausted than when I went to sleep impotence and frigidity There is a falling off in the accustomed standards of adequacy and efficiency The sufferer finds himself unable to make decisions in business or personal life he is beset by fears which he realizes are not entirely valid he seems disinclined to pursue the usual social activities and prefers to be left alone he finds social intercourse a strain and conversation difficult Finally he decides that he needs a rest or a change he finds that he ought to leave his job get out of a rut or get away from it all

Gradually or sometimes suddenly the depression deepens and the patient feels hopeless and despondent There is a sense of impending disaster which makes the future seem black and the prospect unrelieved By this time the patient looks depressed and miserable The expression is fixed and tight lipped furrows deepen the body seems stooped it is difficult to move and actions become increasingly slow Left to himself the patient may sit for hours without moving Thinking is slow and retarded speech is monosyllabic and there may be total mutism Decisions are difficult to make and painful The slightest detail looms gigantic and is weighted with great emotion Ideas of remorse and self depreciation appear Ancient trivial mistakes are revived and magnified Self accusations are hurled guilt mounts without control delusions of persecution or poverty and hypochondriacal thoughts are frequent

Often the unwillingness to eat produces great loss of weight and a lowering of the basal metabolic rate There may be severe constipation and amenorrhea phenomena which are secondary and not to be inter

Treatment —The schizophrenic is institutionalized for adequate therapy referable to his own problems and for the protection of the immediate family the physician and the community

The modern treatment of schizophrenia requires some form of *shock therapy* through the use of insulin (p 1330) the medullary convulsants or by electrical methods (p 1330) These technics are the province of the specialist and are combined with psychotherapy in the attempt to arrest the process and maintain relatively normal interludes A judicious interweaving of shock and psychoanalytic therapy, in early schizophrenic reactions, accomplishes more than either modality without the other

A surgical approach to the treatment of schizophrenia is the technic of prefrontal lobotomy involving a severance of fiber tracts through a trephine opening An occasional brilliant result is achieved warranting con sideration of the procedure in expert hands

MANIC-DEPRESSIVE INSANITY

The manic depressive psychosis is a highly important and common reaction type It is observed very frequently in general practice and is characterized by phasic episodes of excitement and depression Aside from the more striking examples which constitute 10 to 50 per cent of patients admitted to mental hospitals *masked forms* of the depressive phase are seen with disturbing frequency by the family practitioner

Prepsychotic Personality Types —It is important for the practitioner to recognize the prepsychotic personality types of the manic depressive reac tion He has daily experience with personalities given to wide and unpre dictable swings in mood from gayness to sadness These seem unmotivated by anything in reality and apparently arise without obvious cause

Depressions —Most frequently the practitioner observes episodes of de- pression which recur at irregular intervals and deepen during some part of the day They may or may not be interspersed with periods of elation In these phases common complaints include apathy fatigability lack of pep' disinterestedness the blues loss of ambition and initiative in ability to do intellectual work and loss of potency or appetite Everything seems to be just too much and nothing seems worthwhile

Elations —Less often the practitioner recognizes the hypermanic per sonality characterized by excessive energy constant bustling limitless pep absence of fatigability a superficial interest in a myriad of things readiness for fresh undertakings in business or pleasure and avidity for new experiences thrills excitement or sexual contact

For the most part prepsychotic personality types present no important clinical finding It is only when the degree of involvement becomes suffi cient to interfere with the normal activities of life that the practitioner is consulted At this time prophylactic psychotherapy may be launched particularly in a depression with promise of preventing the development of the fullblown psychosis

Clinical Manifestations of Manic Depressive Psychosis —Most often the manic depressive psychosis arises in the patient with the prepsychotic per sonality type The transition may be as abrupt as the falling of a curtain or it may be imperceptible A brief almost unnoted period of depression

may precede a fully developed phase of excitation Contrariwise the hypomanic may develop irritability and a process of slowing down as if suddenly he were compelled to leave a concrete road and continue his course in heavy sand or mud

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preted as primary or etiologic in their significance In the advanced stages the patient goes into stupor, and psychomotor activity speech and cerebration are suspended

Etiology and Pathogenesis—The etiology of the manic depressive psychosis is unknown *Psychogenic elements* unquestionably play a role The psychoanalytically trained psychiatrists lay emphasis on these factors but most of the eclectic school of neuropsychiatrists regard the disturbance as *metabolic* or *toxic* in origin There seems no doubt as to the existence of a *hereditary factor* since the manic depressive psychoses are twenty five times as frequently observed among the siblings of previous sufferers as in the general population The manic depressive reaction occurs twice as commonly in women When it occurs at the menopausal time it is regarded as an *involutional psychosis* (1372)

Nervous Breakdown —Occasionally there appears an exciting factor such as the loss of a job disappointment in a love affair or a prolonged illness In most of these examples of so called 'nervous breakdown' it is more likely that the apparently causative agent is a precipitant and merely coincided with or provoked the deeper underlying disturbance

In no instance are there any demonstrable pathologic or significant laboratory findings

Diagnosis—A complete diagnostic survey is conducted before subscribing to the diagnosis of manic depressive psychosis The agitated phase may be mistaken for *hyperthyroidism* (p 1197), and the depressed phase is simulated by *hypothyroidism* (p 1191) the early phases of subacute or chronic *infection* particularly *tuberculosis* the premonitory manifestations of chronic and debilitating diseases such as *carcinomatosis pernicious anemia* the *leukemias infectious mononucleosis* and *brucellosis*

In addition to a record of the temperature curve and the completion of a meticulous physical examination the laboratory investigation includes a full blood count urinalysis estimation of the basal metabolic rate radiography of the chest and serologic reactions for syphilis and brucellosis

Course and Prognosis—In contrast to the ominous outlook in the schizophrenic reaction the prognosis in the manic depressive episode holds considerable promise Proportionately only a small percentage of the afflicted develop to the stage where they require institutionalization and treatment often offers a bright if temporary prospect

Treatment—In the treatment of the earlier mild phases of excitement and depression the general practitioner functions quite successfully He comes to the situation with certain distinct advantages since in most instances the patient knows him and as far as his illness permits has confidence in him

Nontechnical Psychotherapy—Especially in the case of a patient with hypochondriacal anxiety a thorough going and complete *physical examination* is an essential first step It must be sufficiently complete to justify the physician s contention that there is nothing organically wrong It should not be too fussy or specialized as to suggest to the already suspicious patient that there is hidden or subtle disease The physician must not expect overmuch from his assurance knowing that his psychotherapeutic effort is opposed by the patient s need or 'will to be ill' He must be prepared patiently to hear out the patient he must be ready to sit

through and be interested in the mass of detail which seems to be so pressing and important to the patient Not infrequently this material contains the clue to an irritant or conflict which can be judiciously dealt with on a superficial basis

The depressed patient s need for reassurance must not be answered by attempts to minimize the complaints or the conveyance of the idea that he is really not as sick as he thinks The patient must not get the notion that a complaint which is very real and disturbing to him is trivial or fictitious to his physician As in any psychotherapeutic relationship the realness of the patient s complaints must be a premise Never should the physician imply that the difficulty is imaginary For indeed it never is! The difference between unreal and imaginary and psychogenic or emotionally induced must be meaningful to the physician if he is successfully to communicate that distinction to his patient

Drug Therapy—Many depressed patients receive a considerable lift from *amphetamine sulfate* given in doses of 2.5 to 10 mg each day The mildly agitated are sedated with *barbiturates* during the day and are given a *hypnotic* at bedtime

Other recommended preparations which probably have no specific value other than through the power of suggestion include *strychnine caffeine neurophosphate thiamine chloride* and others of the vitamins *androgen estrogen adrenal cortical extract* and *epinephrine* In order to encourage the return of the patient for psychotherapy any one of these substances may be injected by hypodermic The physician who highly regards the specificity of the injected product is a better psychotherapist than the skeptic

Hydrotherapy—The ambulatory treatment of the depressed patient is often aided by home *hydrotherapy* (p 3792) The advances in modern plumbing provide for a warm relaxation tub bath a cold shower or shock treatment provided by buckets of cold water

Change in Environment—Every effort should be made to keep the patient in his environment despite his desire to escape and seek other surroundings or another job With continuation of the symptoms and persistent urgings on the part of the patient it may be necessary to yield and agree to a holiday such as a fishing or a hunting trip or a visit to the mountains or the seashore or to relatives or friends A change of job however should not be countenanced until the vacation has been tried

In contrast to the *depressed patient* the *agitated individual must be* prevented from entering upon flamboyant enterprises which may involve the patient his family and friends in financial havoc

Formal Psychotherapy—Formal psychotherapy in an ambulatory fashion is advisable for patients who are not sufficiently ill to require institutionalization and yet who fail to respond to the practitioner s nontechnical endeavors Those who advocate psychoanalysis maintain that their efforts often *control the fluctuation in the manic depression reaction* and spare the patient from the more serious ravages of the disturbance

Institutionalization—Institutionalization is required for the depressed patient when he becomes suicidal or can no longer care for himself In the agitated phases hospitalization is advisable to prevent difficulties resulting from excesses in drinking sexual desire financial investments or gambling

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forgivable sin and cloaked with a profound sense of guilt The personality quirks and eccentricities become accentuated until insight is so far lost that the mental symptoms dominate all thinking and activity

Treatment —The minor personality disturbances of the involutional period are managed in the manner of the *male* and *female climacteric* (p 2523) Fully developed involutional psychoses require *institutionalization* Shock therapy (p 1330) may be of significant value in association with adjuvant psychotherapy and injections of androgen or estrogen

PARANOIA AND PARANOID REACTION TYPES

Psychiatrists dispute the nature of true paranoia in its relation to the paranoid reactions of schizophrenia The present discussion avoids these issues and is content with descriptive detail

Etiology —The etiology of paranoia is unknown Psychogenic elements probably play a large if not exclusive determining role The prepsychotic *personality varies but frequently the illness is encountered in people* who have always been more or less suspicious or mistrustful who have been stubborn and resentful of criticism and have found refuge in sulking or in fantasy life In these patients the psychosis seems but a continuation and acceleration of a customary pattern for dealing with conflicts especially unconscious ones The Freudian explanation for paranoia stresses the role of unconscious homosexuality which is generally accepted as an important element in the production of illness

Clinical Manifestations —The outstanding characteristics of paranoia are the presence of central *delusional themes* most frequently *persecutory* or *grandiose* The *idee fixe* is systematized and unchangeable It develops insidiously unrelated to toxic or organic causes and unassociated with an emotional or intellectual dilapidation of the general personality

The distrust and suspiciousness of the prepsychotic state increases Everything is interpreted by the patient as relating to him (ideas of reference) he finds hostility everywhere the inner tensions increase with ever increasing vehemence and rigidity and his conflicts drive him to defend his delusional patterns Even past events are reinterpreted to fit the delusional need and the patient finds in them evidence of which he had not himself been aware when they were occurring (retrospective falsification)

At first glance the arguments of the paranoiac are beguilingly convincing An attentive hearing however soon reveals weaknesses Although granting the original false premise they proceed *with a certain logic and* plausibility The patient appears too tense too anxious too sullen and uncommunicative when pressed as though in an unconscious sense he was aware of the frailty of his thesis The delusions however are never long subjected to reason and no explanation other than the delusional one is even tenable

In certain types of the paranoid reactions the delusional pattern is accompanied by varying degrees of personality disintegration approaching the status of a paranoid schizophrenia Paranoids confronted with jealousy and hostility not infrequently resort to alcohol See p 3847

Prognosis —Though the paranoid may continue to live a fairly adequate life outside of a hospital recovery never occurs The mild varieties include

Shock Therapy—The depressed phase of manic depressive states responds brilliantly to *shock therapy* using insulin the medullary convulsants or electrically induced seizures Perhaps the best results are obtained by the combination of shock therapy during the height of the psychosis with supportive psychotherapy during the free phases

INVOLUTIONAL PSYCHOSES

It is difficult to estimate the role of endocrine dislocations associated with the climacteric in the causation of involutional psychoses Many psychiatrists believe that separate classification is unwarranted and regard the involutional changes as mere additional strains in the total adjustment of the personality Others interpret the metabolic and hormonal changes as of prime importance in pathogenesis

Clinical Manifestations—A review of the personality of most patients discloses frank signs of prior maladjustments with timid inhibited worr

TABLE 89—RESULTS OF ELECTRIC CONVULSIVE THERAPY IN 800 CASES OF THE AFFECTIVE DISORDERS

	Total	Recovered and Much Improved	Improved	Unimproved
Manic depressive (depressed)	60	52 (86 6 per cent)	4 (6 7 per cent)	4 (6 7 per cent)
Manic depressive (manic)	32	27 (84 4 per cent)	3 (9 4 per cent)	2 (6.2 per cent)
Involutional Melancholia	76	66 (86 9 per cent)	8 (10.5 per cent)	2 (2 6 per cent)
Involutional Paranoid	32	14 (43 7 per cent)	8 (25 per cent)	10 (31.3 per cent)
Total	200	159	23	18

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some frugal overconscientious and masochistic tendencies, compulsive drives rigid attitudes and a deep sense of insecurity The associated climacteric changes superimpose additional psychological stresses which may contribute substantially to the full development of the psychosis

The menopause does have a profound emotional impact on an unhappy insecure woman and failing potency disturbs the man who had never been too secure in his psychosexual adjustments False teachings have much to do with many conflicts especially in women who are brought up to look with dread toward the oncoming change of life and expect the worst who believe the menopause demands celibacy and drive their husbands to continence or philandering Industry with few jobs for men beyond the age of forty adds to the hollowness and insecurity of those who have not been successful in their careers

Characteristic of the involutional psychoses are delusional ideas commonly of a persecutory nature feelings of guilt and self deprecatory ideas The most trifling indiscretion in youth is resurrected interpreted as an un

Metabolic	With avitaminoses diabetes mellitus (p 1246) episodes of hypoglycemia (p 734) renal insufficiency and azotemia (p 2276) hepatic insufficiency and cholemia (p 1953) hypothyroidism and hyperthyroidism (p 1197) and acidosis (p 721) *Get urinalysis blood* chemistry and B M. R. Try therapeutic tests with soluble vitamins iodides and glandular extracts (p 1149)
Pharmacologic	Following therapeutic administration of general anesthetics sedatives hypnotics cocaine opiates atropine scopolamine bromides arsenicals, mercurials and sulfonamides
Toxicologic	In drug addicts particularly with marihuana With lead, mercury manganese and carbon disulfide poisonings in industry In carbon monoxide poisoning
With Multiple Sclerosis	Mental changes in conjunction with temporal pallor of optic disc and diffuse motor and sensory manifestations.
With Hyperchromic Anemia	Mood changes in association with abnormalities of the hemogram (p 1077)
Epileptic	Delusions of persecution and mental deterioration most often precipitated by bromide intoxication

in their roster many of the cranks the habitual litigants the chronic writers of letters to the authorities and press and the alcoholics When the paranoid reaction is a secondary feature as in paranoid schizophrenia *occasional spontaneous but partial remissions may occur*

Treatment —Ambulatory treatment is highly ineffectual *Hospitalization* is required from the point of view of the protection of the community and especially those against whom the delusions are directed shock therapy and prefrontal lobotomy are worthy of consideration if medicolegal barriers can be overcome

TRAUMATIC PSYCHOSES

Traumatic psychoses constitute reactions that occur after injury The trauma may be applied directly to the head or it may be inflicted on other portions of the body Under any circumstance the history usually reveals a *preexistent personality conflict* which under the influence of the traumatic experience becomes activated

Trauma also precipitates clear psychotic reactions The first obvious manifestation of a schizophrenic reaction a manic-depressive psychosis or a general paresis may seem related to injury a fact which is often a subject for violent medicolegal argumentation

Psychoses of Combat —The violence of modern war has added immeasurably to the incidence and importance of traumatic psychoses To the *shell shock* of World War I have now been added the mental disturbances that result from prolonged submersion in submarines from the daily hazards in the merchant marine with the ever present dangers of bombing and torpedoing and from the inhuman conditions in aviation where men travel at phenomenal speeds in and below the stratosphere and where the

DIFFERENTIAL DIAGNOSIS OF

Symptomatic Psychoses

Symptomatic psychoses are differentiated from idiopathic varieties by definite evidence of their cause in the history physical and neurologic status examinations cerebrospinal fluid findings or the electroencephalogram

TYPE	DIAGNOSTIC FEATURES
Traumatic	History of injury Clinical manifestations dependent upon prior personality pattern.
Febrile	Usually associated with acute hyperpyrexia or prolonged and exhausting infection. Acute varieties may become manifest through mania or coma Protracted type often associated with avitaminoses
General Paresis	Syphilitic encephalo meningitis Wassermann tests positive in blood and spinal fluid. Complete decolorization in first five tubes of colloidal gold reaction Associated changes in pupils and deep reflexes Favorable response to specific therapy (p 1379)
Post encephalitic	History of infection with cranial nerve palsies and spinal fluid pleocytosis Manifestations usually involve total personality and sleep pattern
Post meningitic	History of fever with nuchal rigidity headache and generalized eruption Tubercle bacilli or pathogenic cocci isolated from cerebrospinal fluid (p 3737)
Choreic	Behavior disorders associated with choreiform movements and evidences of carditis Sedimentation time usually increased (p 190)
Neoplastic	Various psychotic reactions may accompany brain tumor Make complete survey including neurologic status (p 3584) fundus examination (p 1545) spinal fluid studies (p 3737) ventriculogram (p 3783) electroencephalogram (p 1406) and exploratory craniotomy if necessary
Pre senile Psychoses	Occurs between ages of 40 and 60 Associated with other evidences of arteriosclerosis particularly retinal changes hypertension and nephropathy
Senile Psychoses	After 65 Accentuation of personality defects Usually associated with weight loss and manifestations of generalized arteriosclerosis (p 1382)
Post apoplectic	History of cerebral accident usually hemiplegia (p 1439)
Cardiovascular	In association with backward failure (p 941) pericardial effusion (p 1008) acute and chronic pericarditis (p 1010) and cardiac tamponade (p 872)

Metabolic	With avitaminoses diabetes mellitus (p 1246) episodes of hypoglycemia (p 734) renal insufficiency and azotemia (p 2270) hepatic insufficiency and cholemia (p 1953) hypothyroidism and hyperthyroidism (p 1197) and acidosis (p 721) Get urinalysis blood chemistry and B M R. Try therapeutic te ts with soluble vitamins iodides and glandular extracts (p 1149)
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human economy is subjected to the pitiless strain of going into and out of power dives"

Clinical Manifestations—The clinical manifestations of the traumatic psychoses depend in great part upon the personality pattern that preceded the traumatic experience There may be excitation and mania or depression and coma

The psychosis is often followed by late personality disturbances after the patient is considered well He becomes irritable nervous fearful apprehensive sleepless depressed and moody He suffers from headache fatigue lack of concentration or the will to work He smokes excessively, and soon begins to take too much coffee benzedrine alcohol and barbiturate and too little food

The post traumatic period is also followed by moral and social deterioration Disturbances in sexuality are observed as well as a general mental impairment A familiar illustration of the latter is the syndrome of 'punch drunk seen in pugilists

Diagnosis—The diagnosis of traumatic psychosis is the province of the *specialist* especially in compensation and liability suits

Treatment—The treatment of the traumatic psychosis is *specialist province* under *institutional* auspices It involves a complex program including psychotherapy reeducation and revaluation hypnagogic reverie physiotherapy hydrotherapy occupational treatment and rehabilitation features Since the prognosis varies between complete recovery and more or less invalidism the efficacy of any therapeutic modality is difficult of evaluation The practitioner who assumes responsibility for his patient is subjected to a thankless criticism and the nuisance and embarrassment of the litigious features

FEBRILE PSYCHOSES

Pyrexia and hyperpyrexia often are associated with psychiatric derangements Adult patients with systemic infections become drowsy and comatose disoriented restless or delirious To add to diagnostic difficulties infants and children are prone to develop convulsions See p 2780

Clinical Manifestations—Most commonly the febrile psychosis occurs *at the onset* of an acute episode of hyperpyrexia Next in frequency the psychosis is encountered in the *long fevers* when metabolic derangement cumulative drug poisoning exhaustion and vitamin deficiencies are added to the disturbances of the febrile process The febrile states commonly associated with psychoses include pneumococcus pneumonitis typhoid fever and prolonged sepsis usually of streptococcal origin

The occurrence of psychiatric symptoms in a course of a febrile disease suggests possible infectious invasion of brain tissue When convulsions are added to the other disturbances a *lumbar puncture* is indicated for diagnostic and therapeutic purposes

Prognosis—The febrile psychosis that occurs early in a disease does not add appreciably to the gravity of the prognosis The late psychosis is an evil prognostic omen partially because it indicates a severe reaction and partially because it interferes with nursing care The febrile psychosis rarely produces permanent disturbances When protracted derangements occur there is a strong likelihood that a personality disorder preceded the

infection and that the psychosis was precipitated rather than was caused by the acute illness

Treatment—The febrile psychoses are treated with a minimal use of drugs Constant observation by experienced nurses is mandatory since patients may cause irreparable damage by leaving bed tearing off dressings and *intravenous infusion sets and by pulling out catheters and drainage tubes* Serious injuries of course result when patients fall out of bed or jump from windows

Such disturbances are best controlled by *hydrotherapy* Sponges the application of ice bags to the head and the calming influence of a conscientious and intelligent nurse often suffice for sedation As soon as possible a continuous *intravenous drip* is instituted and the administration of fluids with dextrose saline and the soluble vitamins often gives amazing and seemingly specific relief If these measures alone do not suffice for sedation *paraldehyde* in a dose of 1 to 4 cc is injected into the rubber tubing to produce an immediate and often reasonably prolonged sleep When the patient shows signs of renewed restlessness a further dose of paraldehyde is given

Should the paraldehyde fail to be effectual *soluble barbiturates* (p 3839) are employed The use of morphine and related substances is hazardous since many delirious patients are actually suffering a cat reaction as the result of previously administered opiate See p 3658

SYPHILITIC PSYCHOSES

Syphilis of the encephalomeningeal structures most commonly produces the *syndrome of general paresis* Additionally however there are observed nonparetic syphilitic disturbances such as *taboparesis* and *interstitial vascular meningeal* or *gummatous* changes in the brain tissues

GENERAL PARESIS

The symptoms of paresis usually follow the acquisition of the primary lesion by an interval that may be as brief as five years and as long as twenty five years The peak of incidence is between thirty five and forty five years of age and the frequency of the disease may be estimated from the fact that it constitutes 8 per cent of all first admissions to mental hospitals This does not represent the total figure for the disease since early cases are increasingly being treated in general hospitals

It is likely that the spirochete invades the brain at the time of the secondary stage The spinal fluid findings then are positive What it is that produces the period of latency and what activates the disturbance at the present time remain unanswered See p 340

Pathology—The brain in general paresis is small and atrophic especially over the frontal lobe The dura is thickened edematous and firmly attached to the skull There may be a subdural hemorrhagic pachymeningitis The leptomeninges are cloudy and the arachnoid is firmly attached to the pia External and internal hydrocephalus produce flattening of the gyri and widening of the sulci The dura is infiltrated with new connective tissue and the pia is invaded by lymphocytes and mast cells The adventitial spaces contain lymphocytes plasma and giant cells and to some extent the infiltrations extend free into the tissues Blood vessels are in

human economy is subjected to the pitiless strain of going into and out of 'power dives"

Clinical Manifestations —The clinical manifestations of the traumatic psychoses depend in great part upon the personality pattern that preceded the traumatic experience There may be excitation and mania or depression and coma

The psychosis is often followed by late personality disturbances after the patient is considered well He becomes irritable nervous fearful ap prehensive sleepless depressed and moody He suffers from headache fatigue, lack of concentration or the will to work He smokes excessively and soon begins to take too much coffee, benzedrine alcohol and bar biturate and too little food

The post traumatic period is also followed by moral and social deteri oration Disturbances in sexuality are observed as well as a general men tal impairment A familiar illustration of the latter is the syndrome of *punch drunk* seen in pugilists

Diagnosis —The diagnosis of traumatic psychosis is the province of the *specialist especially in compensation and liability suits*

Treatment —The treatment of the traumatic psychosis is *specialist province* under *institutional* auspices It involves a complex program in cluding psychotherapy reeducation and revaluation hypnagogic reverie physiotherapy hydrotherapy occupational treatment and rehabilitation features Since the prognosis varies between complete recovery and more or less invalidism the efficacy of any therapeutic modality is difficult of evaluation The practitioner who assumes responsibility for his patient is subjected to a thankless criticism and the nuisance and embarrassment of the litigious features

FEBRILE PSYCHOSES

Pyrexia and hyperpyrexia often are associated with psychiatric derange ments Adult patients with systemic infections become drowsy and coma tose *disoriented restless or delirious To add to diagnostic* difficulties in fants and children are prone to develop convulsions See p 2780

Clinical Manifestations —Most commonly the febrile psychosis occurs *at the onset* of an acute episode of hyperpyrexia Next in frequency the psy chosis is encountered in the *long fevers* when metabolic derangement cumulative drug poisoning exhaustion and vitamin deficiencies are added to the disturbances of the febrile process The febrile states commonly associated with psychoses include pneumococcus pneumonitis typhoid fever and prolonged sepsis usually of streptococcal origin

The occurrence of psychiatric symptoms in a course of a febrile disease suggests possible infectious invasion of brain tissue When convulsions are added to the other disturbances a *lumbar puncture* is indicated for diag nostic and therapeutic purposes

Prognosis —The febrile psychosis that occurs early in a disease does not add appreciably to the gravity of the prognosis The late psychosis is an evil prognostic omen partially because it indicates a severe reaction and partially because it interferes with nursing care The febrile psychosis rarely produces permanent disturbances When protracted derangements occur there is a strong likelihood that a personality disorder preceded the

patients treated later the recovery rate falls to 30 to 35 per cent but the progress of the disease is checked in another 30 per cent

Treatment—In the era that preceded the introduction of penicillin in the treatment of syphilis the management of general paresis was conducted with eminent satisfaction through the use of hyperthermia With the combination of the two effective modalities even greater promise of significant therapeutic accomplishment is imminent

Penicillin—Particularly in asymptomatic paresis and in early manifestations of the disorder main reliance may be placed on penicillin therapy given intensively over a brief period of time Re-treatment at stated intervals may be required until greater knowledge of this extraordinary substance has been amassed For an initial course no less than 10 000 000 units of penicillin may be given by introducing 150 000 units intramuscularly every three hours for a period of slightly less than ten days Until more definite long term information is available the practitioner must be guided by the efficacy of this probatory course If spinal fluid clearing is not satisfactory at the end of three months the course must be repeated using perhaps 16 000 000 units in the same period of time This can be accomplished by increasing each individual injection to 200 000 units given at three hour intervals for an eight day period Whether more can be accomplished by a continuous intravenous drip of even more massive unitage remains for the future to decide

Hyperthermia—In institutional practice the experienced expert utilizes *cabinet treatment* In localities where hypertherms are not available fever therapy is accomplished by *blanket wrapping intravenous injections of typhoid vaccine* or the production of a *therapeutic malaria* (p 509) The first two technics are more strictly within the realm of the practitioner who rarely has access to a supply of tested malarial blood

BLANKET WRAPPING—Blanket wrapping is accomplished without the necessity of purchasing supplies that are not accessible in the ordinary home The patient puts on long woolen socks and gets into a bed which has been protected with a large rubber sheet and a length of canvas He is wrapped with several thin blankets and a heavy woolen one Each limb the trunk and shoulders are individually encased and finally the canvas and rubber sheets are drawn around and held together so that only the face is exposed The oral temperatures and temporal artery pulses are recorded at thirty minute intervals Following each reading the patient takes a tumblerful of hot lemonade containing 0 6 per cent of sodium chloride and sugar to taste

With this technic a temperature of 102.2 F is usually reached in three or four hours and 104° F in five to six hours An attempt is made to maintain the hyperpyrexia between 104 and 105° F for six hours At the height of the fever restlessness may be controlled by the administration of morphine or liberal doses of a hypnotic

The blankets are loosened and the patient is cooled if the temperature rises above 105° the pulse rate exceeds 140 or the respiratory rate advances beyond 28 per minute Treatments are repeated at weekly intervals and their efficacy is judged by clinical and serological alterations

INTRAVENOUS TYPHOID VACCINE—The second available method for the production of hyperpyrexia under the conditions of clinical practice con

creased and new blood vessel formation is visible The ganglion cells are severely damaged, the microglia are tremendously proliferated and many rod and "gitter cells" are observed There is an increase in the iron content of the brain tissue the microglia and adventitial cells Spirochetes are found scattered throughout the brain largely in the gray matter

Clinical Manifestations —The clinical manifestations of general paresis include changes in emotional stability intellect and character Patients are frequently depressed with or independent of expansive moods Intellectual impairment is especially marked in the spheres that require attention concentration, mathematical calculation and memory for recent events Personality quirks become accentuated A common symptom is inability to remember what was said or done a few moments previously

Character changes are pathognomonic and occur early in the disease They may take the form of sudden streaks of unwarranted extravagance carelessness about personal hygiene in a previously fastidious individual unaccustomed sexual promiscuity excessive alcoholism or criminal behavior in a previously conformant personality

In addition to the psychogenic symptoms there may be physical manifestations such as excessive fatigability headache epileptic seizures speech difficulties incoordination of motor movement (so that the patient is unable to perform simple acts such as buttoning of clothes) unexplained elevation of temperature apoplectiform seizures and alterations in urination and defecation

Physical Examination —Physical examination of the paretic is usually characteristic There is loss of facial tone and a washing out of expression The pupillary reactions reveal the *Argyll Robertson changes* (p 1534) Often there are ocular and extra ocular muscle weaknesses tremors of the face and tongue incoordination and ataxia of the fingers speech defects such as slurring and elision of syllables and absent tendon reflexes Babinski reflexes are frequently found hypalgesia over nose and chest is common and there may be a malar flush in contrast to the pallor of the tabetic

Laboratory Data —The diagnosis of general paresis is clearly revealed by the laboratory data Usually the *blood tests* are positive as are the *spinal fluid reactions* Additionally the *colloidal gold reaction* reveals complete decolorization in the first five tubes The presence of the "paretic curve" establishes or refutes the diagnosis of general paresis beyond the shadow of doubt

Course and Prognosis —Untreated general paresis is a progressive disease Intellectual impairment progresses to a true dementia and expansive paranoid and somatic delusions develop along with disorientation in all spheres The expansive phase which is unduly emphasized is not as frequent or as characteristic as has been generally supposed The emotional reactions deepen with increasing depression elation or agitation The patient becomes unable to care for himself and is utterly confused disoriented and incapacitated Death usually occurs within two or three years after the first symptoms occur

Spontaneous remissions are experienced in a small number of cases and may last from a few months to five years With adequate treatment in a relatively early stage from 30 to 60 per cent of paretics are well enough to return to their usual occupations In the more advanced instances of

ENCEPHALITIC PSYCHOSES

Mental symptoms appear in acute and subacute lethargic encephalitis (p 449) In the actue stage the symptoms are those of any acute toxic infection with *delirium* predominating There is often interference with the *sleep pattern* and the manifestations may vary from intractable insomnia to prolonged somnolence Occasionally the clinical picture simulates that of the schizophrenic or the manic depressive reaction types

In the subacute or chronic phase especially in children there occur devastating *personality alterations* The child exhibits behavior disorders periods of depression and exaltation irritability loss of interest impulsive and uncontrolled antisocial behavior such as lying stealing running away from school and home or gross sexual offenses These children may become very obese or pitifully emaciated

The prognosis of post encephalitic psychoses is never good *Institutionalization is usually required owing to the difficulties that arise at home* and in school

PSYCHOSES FOLLOWING TUBERCULOUS AND OTHER FORMS OF MENINGITIS

With meningeal involvement whether due to the tubercle bacillus or the coccal forms (p 1462) there may be acute delirium periods of irritability and excitement and acute confusional states

In the insidious infections such as *chorea* initial symptoms may be *behavior disorders* such as excessive and unaccustomed sulking temper tantrums and disobedience (p 1359)

PSYCHOSES IN NEOPLASTIC DISEASE

In an alarming number of cases in which patients were admitted to psychiatric institutions for psychotic reactions autopsies have revealed unsuspected silent *brain tumors* (p 1419) *The psychotic patient is entitled* to a complete organic survey with spinal fluid examinations encephalograms ventriculograms electro encephalograms and if necessary an exploratory craniotomy

PRESENILE PSYCHOSES (PICK ALZHEIMER)

Presenile psychoses are relatively rare They occur characteristically between the ages of forty and sixty and run a rapid course ending in dementia and death

The *symptoms* of the psychosis are variable and depend upon the nature and location of the vascular lesion and the personality type that predisposes to the lesion In addition to alterations in the personality panel there may be focal manifestations such as aphasia apraxia or motor and sensory manifestations

The diagnosis of presenile psychosis is made by exclusion The syphilitic derangements are eliminated if the blood and spinal fluids are clear Inflammatory diseases produce cytologic manifestations in the spinal fluid The suspicion of brain tumor requires specialist consultation and exploratory craniotomy

The prognosis of the presenile psychoses is hopeless There is no form of treatment other than custodial care

sists of intravenous injections of typhoid vaccine The usual commercial typhoid vaccines contain 1 000 000,000 organisms to the cubic centimeter An initial injection should not exceed 10 000 000 organisms or 0 1 cc of a 1 10 saline dilution Subsequent doses are dependent upon the reaction to the trial amount

The injection of typhoid vaccine is given in the morning In the suit able reaction the patient has a chill within thirty minutes to two hours The temperature rises to 102° to 105° at which time a second injection using the same dose is administered An adequate response is one in which there is a minimal rise to 104° but a temperature of 107° should not be exceeded

Medicolegal Aspects—In a certain number of instances head trauma activates the symptoms of general paresis and medicolegal controversies arise Not infrequently the precipitating accident resulted from a defect in judgment that was itself an expression of the disease

JUVENILE PARESIS

General paresis occurs as the result of *congenital syphilis* The usual age of incidence is five to twenty five years and this complication is noted in perhaps 1 per cent of all afflicted

The general findings are similar to those in adult paresis except that many of the patients remain *feebleminded* and the course of the disease despite therapy, is almost always progressive As a rule the patient suc cumbs four to five years after the onset of symptoms with confusional states apoplectiform seizures or from intercurrent infection

TABOPARESIS

The coexistence of tabes dorsalis and general paresis is not infrequent the patient revealing the signs and symptoms of both afflictions *Treat ment* is directed along the lines of otherwise uncomplicated paresis (p 1379)

OTHER SYPHILITIC PSYCHOSES

In addition to the syndrome of general paresis the syphilitic brain suffers parenchymatous involvements due to vascular meningeal and gum matous changes Each of these alone or in combination may produce men tal changes of great variety These manifestations usually occur two to five years after the primary lesion

The clinical manifestations are varied They may consist of delirium with a defect in memory for recent events there may be alteration in mood toward depression or euphoria and with increased intracranial pres sure stupor may occur preceded by a state of dullness and apathy In the last circumstance the usual organic findings of increased intracranial pres sure are observed These include papilledema localized nerve palsy (par ticularly of the eye muscles) and a marked lymphocytic reaction in the spinal fluid

The prognosis of nonparetic syphilitic psychotic reactions is somewhat better than that of general paresis Specific *treatment* with or without hyperpyrexia often causes prompt disappearance of the disturbance (p 1379)

PSYCHOSES ASSOCIATED WITH ENDOGENOUS METABOLIC CONDITIONS

Psychoses may accompany a variety of endogenous metabolic conditions The febrile and post febrile *psychoses have been previously mentioned* Psychogenic derangements occur also in *hyperglycemia hypoglycemia acidosis azotemia hepatic insufficiency hypothyroidism hyperthyroidism* and *adrenal cortical deficiency* They are also seen in the *anoxemic states* that accompany *cardiac failure* and in *cardiac tamponade* due to a rapidly accumulating *pericardial effusion*

Psychoses accompany the *avitaminoses* particularly *pellagra* Almost 10 per cent of pellagrins show mental changes which may vary from deliria which are the most common to typical organic psychotic reactions Changes in mood especially depressions are common

The *treatment* of the psychoses is subservient to the correction of the more fundamental disturbance

PSYCHOSES ASSOCIATED WITH EXOGENOUS METABOLIC CONDITIONS

Psychoses develop from the administration of *drugs* and exposure to *chemicals* in industry Among the causative or provocative agencies are alcohol cocaine morphine barbiturates marihuana lead mercury arsenic sulfa drugs atabrine and bromides

BROMIDE INTOXICATION

The indiscriminate use of bromides available to the laity without prescription results in the superimposition of a drug psychosis on the structure of underlying mental or nervous diseases particularly epilepsy or alcoholism Along with the mental symptoms there may be a *bromide eruption* (p 3330) the breath has a characteristic sweetish odor the speech is thick and slurred there is general muscular incoordination ataxia tremors of the fingers and perioral muscles the pupils are widely dilated and react poorly to light and the deep reflexes are depressed or abolished

Treatment consists of stopping the drug forcing fluids and giving large quantities of sodium chloride if necessary by intravenous drip (p 3775) If the restlessness and excitement are intense paraldehyde is the most useful drug to use

PSYCHOSES DUE TO INGESTION OF HEAVY METALS

Psychotic reactions resulting from *lead* poisoning were once frequent At times plumbism produced a quite typical acute delirium and a slowly progressive intellectual dulling leading to a profound mental deterioration Less often there was an obscure mental reaction resembling neurasthenia with irritability restlessness easy fatigability feelings of depression and anxiousness

Similar clinical pictures result from poisoning with *mercury manganese* and *carbon disulfide* (p 747)

PSYCHOSES DUE TO GASES

Compared with the large number of *carbon monoxide poisonings* mental symptoms are relatively uncommon and usually occur only after pro

SENILE PSYCHOSES

Older people are expected to become increasingly egocentric They are apt to be fussy and irritable, and they expect and demand a great deal of attention They become less punctilious about their habits and their personal hygiene and they are forgetful and given to long winded reminiscences

Clinical Manifestations —The normal phenomena of the process of aging usually occur at the ages of from sixty to sixty five When the transition occurs at an early time or develops acutely, the condition is regarded as abnormal in the quantitative sense The forgetfulness develops into a loss *of memory for most recent events the reminiscing becomes an endless* repetition of ancient happenings detailed in the greatest degree, the egocentricity and irritability assume definite paranoid colorings and there are outbursts of unprovoked temper and childish sulking

The paranoid ideas lead to quarreling distrust of family and friends and reluctance to eat and compensatory protective reactions There is a hoarding of worthless objects such as matches pieces of string and left over food These patients wander from home they are improperly dressed they neglect toilet habits and personal cleanliness they become preoccupied with sex and make indecent propositions and expose themselves inordinately as though these practices compensated for lost sexual capacity Often they return to masturbation and puppy love confabulation is common and true delirium confusional states and delusional trends may occur

Treatment —As long as senile patients can be tolerated and cared for at home they are best taken care of under their normal surroundings Essentially, they need patience tact and understanding When the household becomes too greatly disorganized it is wiser to advise institutionalization as one old person may become a wasteful and debilitating burden to an entire family group It is often very difficult to bring the family to hospitalize older people for understandable emotional reasons though it is obvious that the patient would be better managed and happier in the objective atmosphere of a properly equipped hospital

The old person who is kept at home and whose thinking processes are clouded is actually made unhappy in the presence of those with whom he has had previous association at a higher level of intellectuality The contrast keeps him in a state of constant helpless frustration and adds immeasurably to suffering When such a one is placed in a quiet nursing home where he may enjoy comfortable solitude among contemporaries who have likewise passed their peak he lapses gratefully into a state of torpor which is infinitely more merciful and kindly than the feeling of competition in the home

POST-APOPLECTIC PSYCHOSES

Following cerebral accidents patients usually suffer mental deterioration and may become psychotic The management of these problems differs in no wise from that of the senile psychosis except that there may be such additional organic symptoms as pain urinary retention or incontinence

Course and Prognosis—The delirium usually lasts from three to six days Modern treatment has gone far to reduce the mortality which previously was as high as 10 per cent The greatest risks arise from complications especially infections and cardiorenal disease Amnesia for events occurring during the attack is usual

Treatment—The most urgent need is for fluid replacement and the administration of large amounts of vitamin B complex and salt A slow continuous intravenous drip of physiologic saline solution is set up and the soluble vitamins are introduced Sedation is used only when necessary and then judiciously As soon as possible a high caloric vitamin rich diet is given

Korsakoff Syndrome—Korsakoff syndrome is not limited to alcoholics but may be found in other toxic states and cerebral atherosclerosis In the alcoholic it commonly develops after an episode of delirium tremens

The characteristic change is the loss of memory for recent events retention of memory for remote events and a marked degree of confabulation The patient is disoriented especially as to time The mood is characteristically happy and expansive as reflected by the confabulation The patient confined to bed tells of luxurious parties plays he has seen in the company of elegant friends and so forth Insight is usually lacking *There are usually associated peripheral neuritides ocular palsies and nystagmus*

The acute symptoms usually last from four to six weeks Permanent residual damages are not however infrequent and may include memory defects and emotional and intellectual deterioration

Korsakoff's psychosis is treated in the manner of a delirium tremens Proper orthopedic care is given to prevent wrist and footdrop

Chronic Alcoholism—The chronic drinker who uses large amounts of alcohol develops a slow deterioration of the personality in all its spheres Intellectual keenness and perceptibility are dulled and the character is blunted especially in its ethical and esthetic aspects Psychosexual adjustments are especially liable to show deteriorating aspects such as promiscuity exposure and other sexual indecencies

The development of paranoid states is so common that some psychiatrists prefer a separate classification of *alcoholic paranoia* Psychologically this frequent association of alcoholism and paranoid delusions offers provocative spheres for speculation since the mechanisms involved in both conditions include the elements of repressed homosexuality and profound inferiority feelings Lying uncontrolled impulsive behavior personal carelessness and a deterioration of all social sense and responsibility are common The mood may vary between euphoria and depression with great irritability and hostility The usual lay portrait of the chronic alcoholic who is cruel and neglectful of his family but gay and charming when drinking with his fellow topers is fairly accurate

Treatment—Chronic alcoholism represents a chronic profound disturbance of the personality It requires *institutionalization* with the most thoroughgoing psychotherapy Ambulatory treatment is to no avail since short periods of abstinence are followed almost inevitably by recurrences

Psychoanalysis conducted in the protective confines of a suitable hospital is claimed to be helpful in perhaps 40 per cent of cases The results

found and lasting unconsciousness In the acute stages sometimes within twenty four to forty eight hours of the exposure to the gas a severe delirium may occur In other cases, a free period of several weeks may follow the comatose period before the onset of mental symptoms such as confusional states memory defects motor paralyses sensory changes and speech disturbances Rarely do intellectual and emotional defects persist

ALCOHOLIC PSYCHOSES

The general problem of alcoholism is elsewhere discussed (p 1385) There seems little doubt that the alcoholic begins his career as one suffering from a basic and profound personality disturbance Following the inordinate use of alcohol there result metabolic disturbances such as dehydration salt depletion and vitamin deficiencies which complicate the symptomatologic picture and contribute greatly to the clinical manifestations

Certain distinct clinical entities are recognizable in the alcoholic psychoses These include delirium tremens the Korsakoff syndrome chronic alcoholism acute alcoholic hallucinoses and pathologic intoxication Psychotic manifestations that persist after alcohol has been stopped may represent avitaminoses and should be treated appropriately with thiamine niacin and riboflavin (p 616)

Delirium Tremens —Delirium tremens is rarely encountered in patients under thirty It usually follows a prolonged unaccustomed debauch but may be seen in chronic alcoholics It may be precipitated by injury or intercurrent infection It was previously believed that delirium tremens could be induced in a chronic drinker by the sudden withdrawal of alcohol (so called abstinence delirium') but this is probably not true In recent years more emphasis has been laid on the etiologic role of metabolic physicochemical and vitamin factors though the etiology is still obscure

Clinical Manifestations —The delirium is usually preceded by sleeplessness and anorexia heightened irritability terror dreams and a growing feeling of apprehension The patient is increasingly fearful and starts at a trifling unexpected sound The delirium is usually intense visual hallucinations are characteristic such as seeing snakes and repulsive animals and tactile (vermin crawling on the skin) and occupational hallucinations are common The mood is generally one of terror although occasionally the patient is exhilarated expansive and in exaggerated good humor The patient is usually confused and disoriented in all spheres Misidentification of people is common and attention is most difficult to maintain Extreme suggestibility is usually present especially as to sensory impressions The patient is restless cannot sleep and is difficult to keep in bed

Physical Examination —Physical examination usually reveals marked inanition and dehydration The breath is foul and the lips are covered with crusts The face is flushed the lips dry and the pupils widely dilated Tremors of the hands accentuated on intention of the tongue lips and perioral muscles are present Speech is thick and indistinct The temperature is elevated and the pulse rapid and thready Albuminuria is common The nerve trunks and muscles may be tender Unless a complicating neuritis has abolished the deep tendon reflexes they are usually increased

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depend among other factors on the type of personality and the duration of the illness *Shock therapy* has proved valuable particularly when combined with psychotherapy The use of emesis as a *conditioned response* has been reported to 'cure about 40 per cent of a series of more than 800 patients observed for four years Large doses of vitamin B complex are given parenterally and orally for elimination of the deficiency factor

Acute Alcoholic Hallucinosis—The acute alcoholic hallucinosis is a state which usually follows excessive indulgence and consists of auditory hallucinations accompanied by *intense fear The voices usually are of an accusing* and threatening nature and their content reveals much of the unconscious conflict involved in alcoholism There may be olfactory and visual hallucinations as well

Illusions ideas of reference and misidentification are common Delusional states usually paranoid may develop The mood is one of fear apprehension and panic In these moods suicide is not infrequently attempted so that patients should be promptly *hospitalized*

Pathologic Intoxication—Pathologic intoxication occurs in a neurotic or psychopathic individual following the drinking of a trivial amount of alcohol The incident predicates more basic conflicts in personality It is distinguished from ordinary drunkenness by its greater severity and the pathologic nature of its manifestation The effect is one approximating an acute delirium The patient is confused hallucinated disoriented and has *temporary delusional ideas The mood is one of intense fear and apprehension* The upset is shortlived lasting rarely more than a day or two There is usually total amnesia following the episode

Treatment consists essentially of inducing sleep after which the attack is usually terminated Since this type of reaction is not a healthy way to attempt to deal with conflict the sobered patient is advised to undertake a more complete consideration of his personality difficulties under the guidance of the specialist

PSYCHOSES DUE TO SULFA DRUGS

Protracted and profound depressions with memory defects occasionally follow administration of sulfonamide drugs (p 94) It is wise to warn the patient concerning the possibility of the development of these reactions, which disappear more rapidly when *thiamine chloride* is injected intravenously in 100 mg doses or when *amphetamine sulfate* is administered orally

PSYCHOSES OCCURRING WITH MISCELLANEOUS DISORDERS

Psychoses are seen in a miscellaneous group of disorders such as multiple sclerosis hyperchromic anemia and epilepsy

Multiple Sclerosis—A number of patients with multiple sclerosis develop mental changes which are variable in type and severity (p 1501) Euphoria a lack of appreciation of the severity of the disease and a good natured acceptance of the affliction are fairly common Other patients are depressed and irritable with intellectual defects impairment of *judgment* and insight inattentiveness delusions and hallucinatory states

Hyperchromic Anemia—The mental symptoms of pernicious anemia may be apparent before the anemia is detectable From 5 to 35 per cent

of patients show minor mental disorders such as mood changes especially apathy and depression disinclination to work easy fatigability mild deliria paranoid states and intellectual deterioration See p 1077

Treatment is directed to the underlying disease

Epilepsy—The psychiatric problems encountered in epilepsy include *psychic equivalents of the epileptic seizure* such as sudden *uncontrolled outbursts of excitement and destructive behavior including homicide* There may be psychotic states characterized by hallucinations especially auditory and delusions of persecution or of a religious nature Periods of *depression and ecstasy not necessarily alternating* and *fugues* are fairly common. Mental deterioration is by no means as common as usually believed and may represent a bromide intoxication The *treatment* of epilepsy is detailed elsewhere (p 1517)

PREGNANCY AND POST PARTUM PSYCHOSES

See pp 2647 and 2720

CHAPTER 66

THE INVOLUNTARY NERVOUS SYSTEM INTRODUCTION PHYSIOLOGY INTEGRATIONS

Phylogeny
Anatomy
Physiology
Nomenclature
Involuntary and Voluntary Nervous Systems
The Involuntary Nervous System and the Emotions
The Involuntary Nervous System and the Hormones
The Involuntary Nervous System and Metabolism
The Involuntary Nervous System and Allergy
The Involuntary Nervous System and Visceral Controls
The Involuntary Nervous System and Psychosomatic Disease
Methods of Examination
Pharmacology of the Involuntary Nervous System
Surgery of the Involuntary Nervous System

Phylogeny—The cells of the involuntary nervous system arise from the cerebrospinal axis Phylogenetically the involuntary nervous system makes its first appearance in the annelid the first phylum in which a vascular system is developed Of the cells of the primitive involuntary nervous system one group retains as its function the transmission of nerve impulses the other develops into chromaffin tissue and acquires secretory activity In higher vertebrates chromaffin cells collect in the adrenal medulla while nerve cells retain their segmental arrangement

Anatomy—The elements of the involuntary nervous system are represented in the cortex diencephalon medulla cord thoracolumbar and craniosacral regions and in the peripheral ganglia and autonomic plexuses

Cortical Centers—The involuntary nervous system probably has its highest motor neurons in the *premotor cortex* More definitive centers are demonstrable in the *diencephalon* (*hypothalamus*) the *medulla* and the *spinal cord*

Hypothalamic Representation—The hypothalamic representation is suggested in several clearly defined clinical disorders such a *paralysis agitans diabetes insipidus* and the *adiposogenital syndrome* The first of these as described by Parkinson is associated with many functional afflictions of the involuntary nervous system such as *sialorrhea* and *oculogyric crises* With disproportionate frequency it coexists with *hyperthyroidism* and instances of *increasing exophthalmos* Diabetes insipidus and the adiposogenital syndrome are commonly regarded as disorders of the pituitary gland but experimental evidence points more clearly to a hypothalamic disorder in which the involuntary nervous system derangement initiates alterations in the metabolism of water fat deposition and gonadal activity

Medullary Centers—The medullary autonomic centers are clearly demonstrable Close to the midline beneath th sylvian aqueduct and the floor of the fourth ventricle there are nucl i which control *respiration salivation pupillary constriction vasomotor activity* and perhaps the metabolism of the *carbohydrat s*

Pathways of Cord—In the spinal cord the autonomic pathways traverse the *central lateral columns* This pathway is made up of ipsilateral and contralateral connections which cross in the brain stem and at various spinal levels Some functions are bilaterally represented while others seem entirely unilateral as in the instance of pupillary dilatation

Afferent Fibers—Visceral afferent fibers enter the cord in the posterior roots Their pathway follows the course of the other neurons which carry *pain* from other portions of the body Their cells lie in the posterior horn and the axons cross in the anterior commissure

to ascend in the opposite spinothalamic tract *Practical application of this information is* utilized in *anterolateral chordotomy* which abolishes most forms of visceral pain provided the section is carried down to the gray matter

The Thoracolumbar Division—The thoracolumbar division of the involuntary nervous system which is adrenergic is represented by a bilateral chain of twenty four *paravertebral ganglia* with their *rami communicantes* Each chain occupies a position lateral to the vertebral column and extends from the base of the skull to the *ganglion impar* at the coccyx

In the neck the ganglia connected with the three highest cervical nerves fuse to form the *superior cervical ganglion* The *middle cervical ganglion* is formed by a coalescence of the fourth and fifth cervical ganglia Just below this there is often an *intermediate ganglion* which is connected with the *inferior cervical ganglion* by two short fibers which encircle the vertebral artery

The inferior cervical and first thoracic ganglia are usually united into a single structure known as the *cervicothoracic or stellate ganglion* The remaining thoracic lumbar and sacral ganglia are much smaller and are subject to many anomalous variations Each however has a common arrangement relative to its communicating rami The *white ramus* which is *preganglionic* connects with the spinal nerves the *gray ramus* is *postganglionic* and passes out to the peripheral structures

The branches of the *upper five thoracic ganglia* are small and supply filaments to the thoracic aorta and its branches and to the bodies of the vertebrae and their ligaments Branches from the *lower seven ganglia* are large and unite to form the great lesser and smallest splanchnic nerves The *great splanchnic nerve* is white and firm and is formed from the fifth sixth ninth and tenth ganglionic branches It terminates in the semilunar ganglion of the solar plexus and distributes filaments to the renal and suprarenal plexuses The *lesser splanchnic nerve* formed by filaments from the tenth and eleventh ganglia and the cord between pierces the diaphragm and joins the aorticorenal ganglion of the solar plexus It communicates in the thorax with the great splanchnic nerve and ends in the solar plexus The *smallest splanchnic nerve* arises from the last thoracic ganglion and pierces the diaphragm to terminate in the renal plexus

The Craniosacral Division—The craniosacral or cholinergic division is represented by the *vagi* and fibers in the *oculomotor facial* and *glossopharyngeal* cranial nerves Communications are also made with the *superior cervical ganglion* and the *carotid sinus plexus*

The vagus gives off the *recurrent laryngeal nerve* above the diaphragm within the thorax connections are established with the *inferior cervical ganglion* and the *cardiac pulmonary* and *esophageal plexuses* Below the diaphragm the *left vagus* sends branches along the lesser curvature to the anterior gastric wall and a large ramus to the *hepatic plexus* The *right vagus* sends fibers to the posterior gastric wall and through the celiac ganglion to the terminal plexuses in the upper abdominal viscera

The sacral representation leaves the spinal cord with the *second to fourth sacral nerves* in the cauda equina The *nervi erigentes* are formed and their postganglionic neurons connect with the intrinsic plexuses of the *genital a bladder* and *rectum*

The Peripheral Autonomic Plexuses—The adrenergic and cholinergic fibers derived respectively from the thoracolumbar and craniosacral portions of the involuntary nervous system combine to form *peripheral plexuses* The most important of these are the *ciliary ganglia* associated with the oculomotor nerves the *superior cervical sympathetic ganglia* involved in the mechanism of pupillary dilatation and palpebral widening the *sphenopalatine ganglion* affected in Sluder's neuralgia the *carotid sinus nerve* which has highly specialized functions for the reflex control of blood pressure cardiac rate and respiration the *anterior and posterior cardiac plexuses* involved in the mechanism of bronchial asthma the *plexuses of Auerbach and Meissner* in the intestines the *phrenic adrenal renal splanchnic ovarian gastric hepatic splenic and superior mesenteric plexuses* which connect with the dorsal vagal ganglia *inferior mesenteric superior hypogastric* and *inferior hypogastric plexuses* involved with the functions of the lower bowel the bladder and the genitalia

The Ganglionic Relay Stations—In the involuntary nervous system the effector cell occupies a position outside the cord to which it is connected by a *preganglionic medullated fib* The migrated cell gives origin to the true effector fiber which is *nonmedullated* and *postganglionic*

Whereas the impulse in the voluntary nervous system may pass from the cerebrospinal axis to the end organ without interruption in the involuntary nervous system it is relayed at the peripheral ganglion The accessibility of the relay station and its pre and post

CHAPTER 66

THE INVOLUNTARY NERVOUS SYSTEM INTRODUCTION PHYSIOLOGY INTEGRATIONS

Phylogeny
Anatomy
Physiology
Nomenclature
Involuntary and Voluntary Nervous Systems
The Involuntary Nervous System and the Emotions
The Involuntary Nervous System and the Hormones
The Involuntary Nervous System and Metabolism
The Involuntary Nervous System and Allergy
The Involuntary Nervous System and Visceral Controls
The Involuntary Nervous System and Psychosomatic Disease
Methods of Examination
Pharmacology of the Involuntary Nervous System
Surgery of the Involuntary Nervous System

Phylogeny—The cells of the involuntary nervous system arise from the cerebrospinal axis Phylogenetically the involuntary nervous system makes its first appearance in the annelid the first phylum in which a vascular system is developed Of the cells of the primitive involuntary nervous system one group retains as its function the transmission of nerve impulses the other develops into chromaffin tissue and acquires secretory activity In higher vertebrates chromaffin cells collect in the adrenal medulla while nerve cells retain their segmental arrangement

Anatomy—The elements of the involuntary nervous system are represented in the cortex diencephalon medulla cord thoracolumbar and craniosacral regions and in the peripheral ganglia and autonomic plexuses

Cortical Centers—The involuntary nervous system probably has its highest motor neurons in the *premotor cortex* More definitive centers are demonstrable in the *diencephalon (hypothalamus)* the *medulla* and the *spinal cord*

Hypothalamic Representation—The hypothalamic representation is suggested in several clearly defined clinical disorders such a *paralysis agitans diabetes insipidus* and the *adiposogenital syndrome* The first of these as described by Parkinson is associated with many functional afflictions of the involuntary nervous system such as *sialorrhea* and *oculogyric crises* With disproportionate frequency it coexists with *hyperthyroidism* and instances of *increasing exophthalmos* Diabetes insipidus and the adiposogenital syndrome are commonly regarded as disorders of the pituitary gland but experimental evidence points more clearly to a hypothalamic disorder in which the involuntary nervous system derangement initiates alterations in the metabolism of water fat deposition and gonadal activity

Medullary Centers—The medullary autonomic centers are clearly demonstrable Close to the midline beneath the sylvian aqueduct and the floor of the fourth ventricle there are nuclei which control *respiration salivation pupillary constriction vasomotor activity* and perhaps the metabolism of the *carbohydrates*

Pathways of Cord—In the spinal cord the autonomic pathways traverse the *ventrolateral columns* This pathway is made up of ipsilateral and contralateral connections which cross in the brain stem and at various spinal levels Some functions are bilaterally represented while others seem entirely unilateral as in the instance of pupillary dilatation

Afferent Fibers—Visceral afferent fibers enter the cord in the posterior roots Their pathway follows the course of the other neurons which carry *pain* from other portions of the body Their cells lie in the posterior horn and the axons cross in the anterior commissure

Cholinergic Division—The cholinergic subdivision is also known as *craniosacral* from its anatomical characteristics and *parasympathetic* in contrast to sympathetic

Adrenergic Division—The adrenergic subdivision is variously described as *thoracolumbar* or *sympathetic* The former label, which contrasts to craniosacral is dependent upon the anatomical distribution of its fibers the term sympathetic deserves to be eliminated since it is used by some writers to refer to the involuntary nervous system as a whole and by others in reference to the adrenergic subdivision

Involuntary and Voluntary Nervous Systems—In broad terms the voluntary nervous system is concerned with adaptation of the organism to its external environment the more primitive involuntary nervous system regulates the adaptation to internal environment Each of these adaptations is dependent upon influenced by and responsive to changes that occur in the other Phylogenically the involuntary nervous system is older and more primitive hence it is likely that the psyche is more influenced by the *involuntary nervous system than vice versa*

Physiologically the clinician observes frequent examples of interplay between *psyche* and involuntary nervous system Hunger contractions of the stomach register as appetite and initiate the desire to seek food but it is equally possible for the odor of fried bacon and freshly roasted coffee to set up hunger contractions in the stomach by way of the olfactory nerve and cerebral association tracts

Though the anatomical sites are not clearly defined there is incontrovertible evidence to attest to *supramedullary representation* of the involuntary nervous system In diseases characterized by *destruction of the cortex* there occur the symptoms of *adrenergic hypothalamic activity such as the increased muscle tonus rigidity flushing and tremor of paralysis agitans* (p 1505) *destruction of the hypothalamus* is associated with profound changes in the metabolism of water (*diabetes insipidus*) in the deposition of fat and gonadal activity (*adiposogenital syndrome*) and under experimental conditions at least *peptic ulcers* may be produced

The Involuntary Nervous System and the Emotions—The relationship between emotions and involuntary nervous system has been described in detail in the consideration of *neuroses* (p 1335) Overt or occult emotions are productive of an *autonomic imbalance* and conversely disturbances of the involuntary nervous system are accompanied by emotional overtones

Stimulation of the involuntary nervous system by the common emotions is everyday experience *Fear causes us to blanch or blush* we experience palpitation tachycardia or elevation of blood pressure we note a desire to urinate or retention of urine some observe movement of the bowels while others experience obstinate constipation there may be manifest rapid respirations or a spell of breath holding Whatever the *individual pattern* may be the syndrome is effected through the mediation of the involuntary nervous system

The opposite face of the coin reveals that autonomic imbalance is productive of emotional disturbances An injection of *epinephrine* sufficient to cause tachycardia and elevation of blood pressure gives rise to the sensations of anxiety and fear clinicopathologically the patient with *hyperthyroidism* (p 1197) is in constant emotional turmoil whether due

ganglionic fibers make possible the surgical approach to problems in which the involuntary nervous system is involved

Physiology—Physiologically the voluntary and involuntary nervous systems differ in that the former *is influenced* by the will and consciousness whereas the latter operates involuntarily and subconsciously The economy of this mechanism must be apparent to the practitioner when he realizes that the vital functions of regulation of heart beat, blood pressure digestive activity and the like proceed during sleep and without trespass upon the conscious functions of the cerebrum Dual innervation, in which both voluntary and involuntary elements participate is required for the socially modified visceral functions of urination defecation and sexual activity Repression of these instinctual propensities is important in the Freudian concept of the neuroses

The Subdivisions of the Involuntary Nervous System—The involuntary nervous system is best divisible according to its pharmacological reactions into adrenergic and cholinergic portions An explanation of the subdivisions has been suggested by Gaskell It is his hypothesis that the ancestor of the vertebrate presented a double segmentation appendiceal and branchial The *branchial segmentation* has given rise to the structures of the primitive endoderm and is concerned mostly with the metabolic functions of gastro-intestinal and respiratory tracts These structures receive augmentor impulses over the cholinergic system, which is stimulated by acetylcholine and inhibitory impulses through the adrenergic system whose stimulant, epinephrine depresses their functional activity

The *appendiceal segmentation* has given rise to the appendages of the skin the subdermal layer of musculature the vascular system and the derivatives of the segmental ducts from which arise the organs of excretion and reproduction Essentially these are concerned with self preservation they receive excitatory impulses via adrenergic system and are inhibited by cholinergic structures

The Tonicity of the Involuntary Nervous System—The involuntary nervous system is in tonic activity The subdivisions are mutually antagonistic and reciprocal in their innervation Paralysis of either one causes overplay as the result of the release of the antagonist.

It has been an easy assumption that *acetylcholine* regulated the normal tonic activity of the cholinergic system and that *epinephrine* functioned similarly for the adrenergic system However the physiological proof of this attractive theory has proved to be more difficult than its enunciation the presence of significant amounts of circulating acetylcholine remains to be proved and epinephrine is not present in the circulating blood in quantities that are anywhere near capable of tonic activity

Emergency Theory—It was the failure of proof of the tonicity theory that led to the substitution of the emergency theory of Cannon This postulated that in times of stress, epinephrine was poured forth to stimulate the adrenergic system This ingenious theory has not been substantiated since it appears that the amount of epinephrine that must be secreted, in order to produce an emergency effect, is beyond the secretory capacity of the gland. Those who have been most concerned with the physiology of the involuntary nervous system have been forced to admit that the theories of tonic or emergency control by known chemical agencies remain to be proved These discussions have more than academic importance as illustrated by surgical attempts to apply the epinephrine theories in practice For example it was the hope that denervation of the adrenal medulla or an almost complete bilateral adrenalectomy might control *hypertension* and *hyperthyroidism* These surgical efforts were unsuccessful as might have been predicated by physiologists more familiar with the fundamental facts

Nomenclature—The involuntary nervous system as a whole is sometimes labeled *autonomic vegetative* or *sympathetic* We prefer the use of the term involuntary since it emphasizes the important physiological differentiation between it and the neurologic mechanisms that are under the control of the will

The subdivisions of the involuntary nervous system are classified by us as *cholinergic* and *adrenergic* This pharmacophysiological terminology refers to the most characteristic features of each of the subdivisions the one is stimulated by *acetylcholine* and drugs of similar activity, the other responds to the effects of *epinephrine*

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to direct action resulting from the metabolic disturbance or through a conditioned reflex or emotion

The "compleat practitioner" must reckon with the *visceral and somatic representations of emotion* and the *emotional overtones of visceral and somatic activities* In each instance the mediation is by way of the involuntary nervous system

The Involuntary Nervous System and the Hormones—Hormonal activity is admittedly under the principal control of chemical and metabolic influences Many clinical observations point to the additional significance of neurogenic mechanisms in the total economy the manifestations of *hyperthyroidism* are obviously sympathomimetic *diabetes insipidus* is frequently initiated by psychogenic factors, fear is often accompanied by *glycosuria* and precedes the onset of many instances of *diabetes mellitus* (p 1246), whose intensity it may markedly increase the syndrome of *anorexia nervosa* is almost indistinguishable from that of total destruction of the anterior pituitary gland (*Simmonds disease*) (p 1169)

The Involuntary Nervous System and Metabolism—There are reciprocally important interrelationships between involuntary nervous system and metabolic phenomena, injections of *epinephrine* produce glycosuria and hyperglycemia the administration of *iodide* results in a striking amelioration of the symptoms of hyperthyroidism (p 1197) *myxedema* is associated with profound changes in subcutaneous tissues lesions involving the *hypothalamus* are characterized by abnormalities in water balance and deposition of fat the rate of *oxygen consumption* and the tempo of *energy metabolism* are strikingly augmented by *sympathomimetic activities* which also increase muscle tone and metabolism

The Involuntary Nervous System and Allergy—The importance of the involuntary nervous system in the pathogenesis of allergy is best illustrated by the relief afforded to *atopic phenomena* (p 547) by injections of *sympathomimetic amines* such as epinephrine angioneurotic phenomena abate the bronchial musculature of the asthmatic relaxes the turgid nasal mucous membrane shrinks and the congested conjunctiva blanches

The Involuntary Nervous System and Visceral Controls—Each tissue or viscus is under the control of the involuntary nervous system to greater or lesser degree *Coordination* is assured through dual and reciprocal innervations transmitted through adrenergic or cholinergic subdivisions which function in a manner that is mutually antagonistic Positive reactions represent the sum of stimulation of stimulator and inhibition of inhibitor negative responses follow inhibition of stimulator and stimulation of the inhibitor In any given instance the end plate may be motor or secretory but the general principle of innervation is uniform

These broad tenets are illustrated more concretely in the digestive and circulatory systems At the sight of food digestive secretions and peristaltic gradient are initiated The bolus is carried down through the esophagus by alternate waves of contraction and relaxation at the sphincters relaxation permits the passage of food through the tract where it is attacked by digestive juices and churned by muscle activity the release of secretin initiates the flow of bile intestinal and pancreatic juices so that these are in readiness for the aliment after it has passed pyloric sphincter when thorough absorption of nutritive material has been ac-

complished and the fecal column reaches the rectum the voluntary nervous system is notified lastly at a proper time and place the stool is expelled as the result of the combined efforts of voluntary contractions of abdominal muscles and involuntary relaxation of the rectal sphincter Consistent with the symphonic concept of involuntary nervous system activities these alimentary phenomena are not solo parts the tissues in which active digestion is occurring require and receive additional quantities of blood through local vasodilatation and engorgement the cardiac rate speeds appreciably during the peak of digestive activity splanchnic engorgement is accomplished at the expense of the efficiency of the cerebrum and voluntary muscles as evidenced by the somnolence and lethargy that follow a hearty meal

Cardiovascular coordinations are equally remarkable Neurogenic or psychogenic stimuli may produce narrowing of the caliber of the arteries blood pressure then rises as the result of which the cardio inhibitor centers effect a compensatory bradycardia To the contrary with dilatation of the peripheral blood bed the systemic blood pressure falls while a central action initiates a compensatory tachycardia Each physiological change is capable of setting in motion registers and brakes of the greatest delicacy so that the total human economy operates silently flawlessly and with incredible efficiency

The Involuntary Nervous System and Psychosomatic Disease—The mutual relationships that exist between psyche voluntary and involuntary nervous system have been previously emphasized Physiologically the voluntary and involuntary nervous systems differ in that the former is influenced by the will and consciousness whereas the latter operates involuntarily and subconsciously For the most part the involuntary nervous system is the ubiquitous and silent partner The more the voluntary nervous system is freed from the insubordinate involuntary system consistently with the harmonious interaction between the systems the greater the advantage to the animal (Gaskell) There are however limits to the tolerance and durability of the involuntary nervous system the demands of civilization may progress (or regress) to the point that this primitive tissue can no longer remain silent under existing conditions It protests by the minor and usually inconsequential symptoms of the syndrome of *autonomic imbalance* (p 1395) More severe or protracted irritation leads to *somatization* and the production of *demonstrable tissue lesions* elsewhere described (p 1344)

Methods of Examination—The involuntary nervous system does not lend itself readily to methods of laboratory investigation The surgeons who have been confronted with the problem of estimating the influences of the involuntary nervous system have devised ingenious indirect methods for approximating the activities of the system relative to the peripheral vasculature and the vasodermal structures

Measurements of *skin temperature blood flow* and *limb volume* are noted before and after *procaine block general anesthesia* and the *intravenous injection of foreign protein* (typhoid vaccine) *oscillometric studies* are made of the accessible arteries of the extremities By indirection an assumption is valid regarding the tonus of the involuntary nervous system as a whole this serves as an index for the probable success of surgical

procedures particularly in hypertension (p 900) and vasospastic disorders (p 791)

Pharmacology of the Involuntary Nervous System —The specific pharmacologic agents whose activities are concerned primarily with the involuntary nervous system include

Cholinergins Acetylcholine, mecholyl doryl pilocarpine physostigmine neostigmine See p 3873

Depressants of the Cholinergic System Belladonna atropine scopolamine homatropine eucatropine novatropine syntropan trasentin See p 3875

Adrenergens Epinephrine ephedrine amphetamine (Benzedrine) neosynephrine, propadrine, paredrine privine kephrine See p 3876

Inhibitors of the Adrenergic System Ergotamine ergotoxine nicotine See p 3883

TABLE 90—SURGERY OF THE INVOLUNTARY NERVOUS SYSTEM

Procedure	Indication
Resection of superior cervical sympathetic ganglion	Facial paralysis for closure of eye (p 1481) Angina pectoris for relief of pain (p 890)
Denervation of carotid sinus	Carotid syncope (p 9??)
Stellate ganglionectomy	Angina pectoris Neuralgias and causalgias of arm or amputation stump Raynaud s disease of arm (p 1000) Hyperidrosis of arm
Preganglionic upper thoracic sympathectomy	Vasospastic disorders of arms
Vagectomy	Peptic ulcer (p 1780)
Supra and infra-diaphragmatic splanchnicectomy	Essential hypertension (p 900) Congenital megacolon (p 1871)
Paravertebral alcohol injection of thoracic ganglia or lumbar ganglia	Cardio aortic pain abdominal pain
Lumbar sympathectomy	Vasospastic disorders of legs spastic paralysis
Presacral neurectomy	Relief of pain
Peri arterial sympathectomy	Raynaud s disease (p 1000)
Peripheral sympathectomy	Peripheral endarteritis (p 994) Thrombo angiitis obliterans (p 1099)

Surgery of the Involuntary Nervous System —The surgical approach to the involuntary system constitutes one of the outstanding achievements of modern times It is quite likely that the accomplishments are as yet only in their first phases but the summary in Table 90 indicates present potentialities

CHAPTER 67

THE INVOLUNTARY NERVOUS SYSTEM PARTICIPATION IN CLINICAL DISTURBANCES

The wide scope of the activities of the involuntary nervous system predicates its participation in the majority of clinical disturbances that affect the human mechanism The most important of these are indicated in Table 91

PRIMARY DISTURBANCES OF THE INVOLUNTARY NERVOUS SYSTEM

In addition to the participation of the involuntary nervous system in many systemic disturbances seemingly primary phenomena are encountered Most often patients suffer the widespread functional disorder of *autonomic imbalance* (p 1395) less often the affliction is more localized as in *carotid sinus syncope* (p 922) the *vasospastic diseases* and the *trophoderms*

VAGOTONIA AND SYMPATHICOTONIA

We do not subscribe to the existence of the distinct clinical entities of vagotonia and sympathicotonia In the former the patient is believed to exhibit the symptoms that are equivalent to an injection of an effectual dose of a cholinergic drug such as physostigmine with resultant bradycardia and intestinal spasmosis In sympathicotonia there are the manifestations that mimic the results of an effectual injection of epinephrine with tachycardia elevation of blood pressure nervousness and palpitation Unfortunately for purposes of classification pure vagotonia and pure sympathicotonia are never demonstrable most patients exhibit evidences of aberrations in the tonus of the involuntary nervous system which we have labeled autonomic imbalance

AUTONOMIC IMBALANCE

In his everyday experience the practitioner encounters widespread disturbances in the realm of the involuntary nervous system Some of the phenomena are completely subjective (nervousness asthenia) while others though lacking evidences of organic disease are objectively apparent

TABLE 91.—PARTICIPATION OF INVOLUNTARY NERVOUS SYSTEM IN CLINICAL DISTURBANCES

Infection	
Typhoid fever	Febrile bradycardia and lymphocytosis
Tuberculosis	Adrenergic flush sweat and tachycardia beyond febrile effect
Allergy	
Urticaria	Relieved by epinephrine
Angioneurotic edema	Relieved by epinephrine
Vasomotor rhinitis	Relieved by epinephrine
Bronchospasm	Relieved by epinephrine
Metabolism	
Hyperglycemia	Produced by epinephrine
Elevation of basal metabolic rate	Produced by epinephrine
Increased oxygen consumption	Produced by epinephrine
Glycosuria	Produced by epinephrine and by injury to central nervous system
Water exchange	Polyuria and polydipsia from lesions of hypothalamus (diabetes insipidus)
Fat deposition	Obesity and genital dystrophy from lesions of hypothalamus (Frohlich s syndrome)
Muscle metabolism	Tremors produced by epinephrine with increased excretion of creatinine
Circulation	
Blushing	Atropine effect
Blanching	Epinephrine effect
Vasospasm with cold extremities to point of gangrene	Ergot poisoning sensitivity to overdosage with ergotamine nicotinism (?) Raynaud s disease (p 1000) with operative relief from sympathectomy
Angiospasms	Produced by epinephrine and nicotine relieved by procaine block and sympathectomy (p 91)
Angina pectoris	Produced by epinephrine relieved by sympathectomy (p 890)
Hypertension	Produced by epinephrine relieved by sympathectomy (p 900)
Bradycardia	Produced by cholinergins (physostigmine) relieved by atropine
Tachycardia	Produced by epinephrine nicotinism (?)
Coronary dilatation	Follows sympathectomy (?)
Cardiac irregularities	Produced by epinephrine relieved by sympathectomy (p 873)
Raynaud s disease	Simulated by ergotism relieved by sympathectomy
Erythromelalgia	Peripheral vascular neurosis"
Acroparesthesia	Peripheral vascular neurosis"
Trench Foot	Peripheral vascular disturbance
Thrombo-angiitis obliterans	Partially simulated by ergotism accentuated by smoking (nicotine)
Blood	
Lymphocytosis	Produced by epinephrine
Eosinophilia	In allergies

TABLE 91—PARTICIPATION OF INVOLUNTARY NERVOUS SYSTEM IN CLINICAL DISTURBANCES (Continued)

Endocrine System	
Hyperthyroidism	Preceded by autonomic imbalance simulated by epinephrine lymphocytosis
D abetes insipidus	Posterior pituitary or hypothalam c lesion
Adiposogenital syndrome (Frohlich)	Pituitary or hypothalamic lesion
Adrenal cortical deficiency (Addison)	Relieved symptomatically by epinephrine
Status thymico-lymphaticus	Lymphocytosis
Diabetes mellitus	Simulated by injections of epinephrine inhib ted by pituitary removal and injury to hypothalamus (Houssay)
Neu ology	
Autonomic imbalance	Functional d sturbances usually on const tutional or emotional bas s often with neuro is (p 133)
Psychosomatic disease	Autonomic imbalance (p 139) with en l-o gan *pathology (p 1314) con tr on hyster a (p 13*73)
Epilepsy	Explosive autonomic seiz ires (?)
Migraine	Dilatation of cerebral vessels
Headache	As migraine (p *1509*)
Paralys s agitans	Central autonom c lesion occasionally with exophthalmos and hyperthy o 1 sm
Hypothalamic d s ase	See I itu tary D so 1 s (p 11 9)
Resp at on	
Vasomotor rhinitis	Allergy rel eved by epin phrine
B onchial asthma	Allergy rel eved by epinephrine
D gest n	
Secretory d sturbances	See Gastr c Secretory Neuroses (p *1 67*)
Motor d turbances	See Card ospasm (p 1723) Gastr c Motor Neuro es (p 1 6) Peptic Ulcer (p 1 30) Pylorospasm Reg onal Il t s (p 1851) Mu ous Colitis (p 1846) Intest nal Neuroses (p 1845) Nonspecif c Ulcerative Colit s (p 18 6) S gmo d Spasm (p 1846) Congen tal Megacolon (p 1871)
U nary System	
Polyur a	See Hypothalamus (p *14 5*)
Bladder innervation	See Retent on of U ine (p 2981) In ontinen e of U ine (p 2 65)
Rep oduct e Syst ms	
Uterus	See Dysmenorrl ea (p 2561) Parturition (p 26 7)
Gen talia	See *Erection (p 240)* Orgasm (p 2490) Fr gidity (p 2391) Impotence (p 2409)
Cl ma t ric	Male (p 2412) and f male (p 2 3) associ te l with manif stat ons of autonomic imbalance

TABLE 91 —PARTICIPATION OF INVOLUNTARY NERVOUS SYSTEM IN CLINICAL DISTURBANCES (*Continued*)

Skeletal and Locomotor	
Tremors	Produced by epinephrine partially inhibited by atropine in hyperthyroidism and paralysis agitans
Muscle dystrophies	Myasthenia gravis (p 2886) relieved by physostigmine (p 2886)
Tegumentary	
Hyperidrosis	Produced by epinephrine
Pilomotor activity	Produced by epinephrine
Cutaneous allergies	Relieved by epinephrine
Cutaneous vascular disorders	Simulated by epinephrine
Cutaneous thermal disorders	Simulated by epinephrine
Eye	
Mydriasis	Produced by instillations of atropine and epinephrine
Miosis	Produced by instillations of pilocarpine and eserine
Enophthalmos	Produced by paralysis of superior cervical sympathetic ganglion
Exophthalmos	Produced by hyperthyroidism through unknown mechanism

(flushing blushing tachycardia diarrhea lability of the blood pressure motor and secretory disturbances of the intestinal tract sweating or tremor)

Autonomic imbalance is a vexing and irritating condition so far as clinical practice is concerned Obviously its production is closely allied to emotional instability the practitioner recognizes that many if not all of its manifestations are seen in the *anxiety neuroses* (p 1347) An understanding of the condition has not been furthered by the dismissal of these complaints as functional neurotic or hypochondriacal or as evidences of larval hyperthyroidism formes frustes of hyperthyroidism basedoid or manifestations of adrenal insufficiency

Etiology —The factors that *predispose* to autonomic imbalance are unknown Most patients note some manifestation as far back as memory exists Certainly the predisposition seems to be inherited or associated with some early environmental factor

The *exciting causes* of autonomic imbalance are more clearly delineated They occur most often during the era of changes in sexuality and are more common at puberty at the menopause and during menstruation More directly however autonomic imbalance is precipitated by *psychic insults* and is associated with the various neuroses (p 1335)

Clinical Manifestation —The clinical manifestations of autonomic imbalance are varied They include palpitation shortness of breath cardiac irregularity particularly premature contractions headache insomnia attacks of diarrhea intestinal spasmoses secretory disturbances of the stomach and intestines menstrual disturbances particularly dysmenorrhea excessive sweating vasomotor instabilities such as blushing flush

ing or coldness of the extremities emotional instability tachycardia bradycardia tremor nervousness and asthenia

The Individual Reaction Picture—Despite the variety in the manifestations of the functional disturbances of the involuntary nervous system each individual has a unique reaction picture Those who suffer from pylorospasm always have pylorospasm and those with tachycardia never develop bradycardia The reaction picture never really disappears but is subject to exacerbations and remissions At any given time it can be activated by fatigue and emotional disturbances such as fear fright anxiety or anger

Laboratory Data—The physical examination of the patient with autonomic imbalance is disturbingly normal With intestinal symptoms roentgenograms reveal only functional disturbances such as excessive motility or spasm gastric test meals show only secretory and motor changes The basal metabolic rate is normal though the clinical symptomatology suggests a hyperthyroidism blood counts occasionally reveal a tendency towards lymphocytosis and an unusual sensitivity is observed to the subcutaneous injections of epinephrine The last previously called the Goetsch test was regarded as pathognomonic of excessive activity of the thyroid gland and an indication for surgical procedures Its nonspecificity is apparent from the fact that at least 33 per cent of normal medical students show the identical response

Diagnosis—The diagnosis of autonomic imbalance is established by exclusion Since adrenergic symptoms simulate hyperthyroidism the estimation of the basal metabolic rate and an adjudication of the response to iodide are warranted before a final opinion is expressed Those patients with gastro intestinal symptoms are entitled to stool examinations and contrast radiography since the manifestations strongly suggest peptic ulcer in many instances

Course—The vast majority of patients with autonomic imbalance learn to live with their functional affliction without recourse to medical therapy Others in association with the *conversion neuroses* (p 1363) progress to the stages of organic disease The *psychosomatic manifestations* which in our opinion are related to the conversion mechanism in hysteria (p 1353) are elsewhere described in detail (p 1344) It is sufficient to state here that they have the three components of psychogenic autonomic and end organ manifestations The last of these is unquestionably a result of the operation of the first two elements Which of these latter precedes the other remains a problem as difficult of solution as that of the determination of the chicken egg sequence

Treatment—The first essential factor in the management of autonomic *imbalance is assurance* that the patient has no organic disease The practitioner must then find time to enter into an explanation of the nature of the disturbance its chronicity its pathologic importance and its relationship to emotional problems

See *Nontechnical Psychotherapy* (p 1316)

Attempts at *specific therapy* usually result in failure Such formidable operations as subtotal thyroidectomy denervation of the adrenal medulla and partial adrenalectomy are ill advised and carry inordinate risk

Specific *pharmacotherapy* is also disappointing except in the instance

TABLE 91 — PARTICIPATION OF INVOLUNTARY NERVOUS SYSTEM IN CLINICAL DISTURBANCES (*Continued*)

Skeletal and Locomotor	
Tremors	Produced by epinephrine partially inhibited by atropine in hyperthyroidism and paralysis agitans
Muscle dystrophies	Myasthenia gravis (p 2886) relieved by physostigmine (p 2886)
Tegumentary	
Hyperidrosis	Produced by epinephrine
Pilomotor activity	Produced by epinephrine
Cutaneous allergies	Relieved by epinephrine
Cutaneous vascular disorders	Simulated by epinephrine
Cutaneous thermal disorders	Simulated by epinephrine
Eye	
Mydriasis	Produced by instillations of atropine and epinephrine
Miosis	Produced by instillations of pilocarpine and eserine
Enophthalmos	Produced by paralysis of superior cervical sympathetic ganglion
Exophthalmos	Produced by hyperthyroidism through unknown mechanism

(flushing blushing tachycardia diarrhea lability of the blood pressure motor and secretory disturbances of the intestinal tract sweating or tremor)

Autonomic imbalance is a vexing and irritating condition so far as clinical practice is concerned Obviously its production is closely allied to emotional instability the practitioner recognizes that many if not all of its manifestations are seen in the *anxiety neuroses* (p 1347) An understanding of the condition has not been furthered by the dismissal of the complaints as functional neurotic or hypochondriacal or as evidences of larval *hyperthyroidism formes frustes of hyperthyroidism* basedoid or manifestations of adrenal insufficiency

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ness or engorgement of the veins An attack may last for one [illegible] days There is no present available form of effectual therapy

NEOPLASMS

On rare occasions *chromaffin tumors* are seen in the structures of the involuntary nervous system These include *neuroblastomas paragangliomas* and *ganglioneuromas* They are discussed in greater detail with the disturbances of the *adrenal medulla* (p 1263)

of the control of excessive vagal activity by the belladonna derivatives Sedation with barbiturates and the use of hypnotics at bedtime tend to take off a good deal of strain Attempts to regulate the involuntary nervous system by *administering hormones particularly those derived from* the sex glands are capable of much more harm than good

DIENCEPHALIC AUTONOMIC SEIZURE

A rare reaction pattern of the hypothalamus is the diencephalic autonomic seizure which consists of *convulsive attacks* of *aura* and *loss of consciousness* The aura is usually a *bitemporal headache* This is followed by loss of consciousness during which there is a sudden diffuse *flushing* or *pallor* of the skin the appearance of a *macular rash* or an *urticaria* on one or both sides of the body The pupils are widely dilated and fluctuate in size, excessive tearing sweating and salivation are noted

Penfield believes that the reaction pattern is hypothalamic and occurs *in association with tumors or affections of the floor of the third ventricle* or neoplasms in the region of the sella The syndrome is specialist province and the patient is referred to the neurosurgeon for more complete study and exploratory craniotomy if necessary

CAROTID SINUS SYNCOPE (VASOVAGAL SYNCOPE)

At the region of the bifurcation the wall of the carotid artery contains a rich plexus of specialized sensory end plates By means of these the carotid sinus nerve joins the glossopharyngeus and the central nervous system With hyperactivity of the *carotid sinus* the patient notes unexplained attacks of *dizziness fainting* and *convulsions* During the seizure the blood pressure falls and the heart rate slows

Attacks of carotid sinus syncope are often precipitated by emotional upset the pressure of a tight collar digital pressure applied for purposes of stopping a cardiac irregularity the pressure of a tumor in the neck or an aneurysm of the vessel Often there is no apparent precipitating factor

Treatment is accomplished surgically by stripping the nerve plexus from the artery at the bifurcation or by section of the carotid sinus nerve The results of therapy are excellent See also p 923

PARALYSIS OF THE CERVICAL SYMPATHETIC (HORNER S SYNDROME)

Paralysis of the cervical sympathetic may follow lesions of the medulla and pons but more often it is due to a tumor or a syringomyelia that involves the first thoracic and eighth cervical roots The Horner syndrome (spinal miosis) consists of *constriction of the pupil narrowing of the palpebral fissure enophthalmos pseudoptosis absence of the ciliospinal reflex flushing of the face and neck* and a local elevation of temperature The oculomotor nerve *is intact the pupils react to light and ptosis can be* voluntarily overcome

The syndrome is not amenable to therapy

HEREDITARY EDEMA OF THE LEGS (MILROY S DISEASE)

Milroy s disease consists of a *chronic circumscribed edema* of both legs It appears soon after birth when a brawny swelling is noted without red

Electroencephalography —Perhaps the greatest advance in neurological diagnosis has been the introduction of electroencephalography This method records the electric potentials that originate from the brain and is similar to electrocardiography The electrodes are placed on the scalp by means

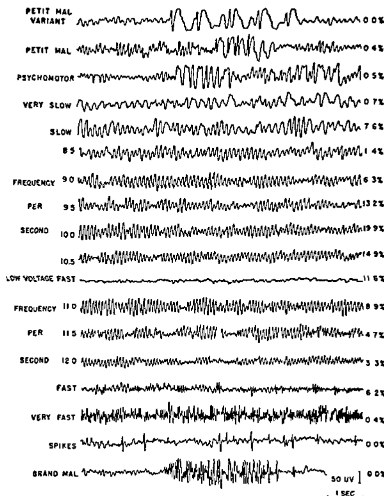


Fig 8—Types of pattern encountered in electroencephalograms in adults The order of arrangement is slow at the top fast at the bottom The top three and bottom two patterns are classed as paroxysmal i e manifesting seizure discharges The names applied to each pattern are shown at the left The percentage incidence of each pattern in the normal control group appears at the right Time and voltage calibrations are given in the lower right corner *

of collodion It is rarely necessary even to cut the hair Through the electrodes the minute scalp currents are amplified by vacuum tubes until they activate an electromagnetic field whose oscillations are noted and written by a pen attached to a sensitive lever

* Gibbs in Manual of Military Neuropsychiatry by Solomon and Yakovlev

CHAPTER 68

THE VOLUNTARY NERVOUS SYSTEM METHODS OF DIAGNOSIS AND TREATMENT

CLASSIFICATION OF THE NEUROLOGIC DISORDERS

Because of the protection of nerve tissue by the bony covering of the cranium and vertebral column primary disorders are of infrequent occurrence the majority of neurologic afflictions represent secondary responses to vascular bacteriologic and metabolic derangements Many syndromes remain obscure and difficult of study and there is a disappointingly long list of purely descriptive conditions of unknown etiology and pathogenesis

The clinical disturbances are classified under the following main headings

Congenital abnormalities
Neoplasms
Circulatory disorders
Trauma and mechanical affections
Infection
Descriptive neurology to include nonbacterial inflammations the scleroses migraine and the epilepsies

NEUROLOGIC DIAGNOSIS

During his routine examination the practitioner notes mental attitudes and aptitudes speech oculomotor activities pupillary reflexes knee-jerks ankle-jerks abdominal reflexes nuchal rigidity motor strength visual acuity and the appearances of ear drums and fundi oculi On indication the deep reflexes are more carefully plotted and a sensory survey is inaugurated with reference to reactions to touch and pain (p 1476) The response to vibration is elicited over the tibias In the presence of positive findings or a suspicion of pathologic invasion particularly by micro organisms the practitioner performs lumbar puncture and has the spinal fluid examined for its cytology bacteriology serology and for the colloidal gold reaction (p 3734) Radiographs of skull and vertebral column furnish additional information

With positive findings neuropsychiatric consultation is mandatory for more refined studies which may include psychometry and electroencephalography The neurosurgeon is brought into the survey for ventriculography encephalography laminography and exploratory craniotomy or laminectomy The ophthalmologist assists by plotting the visual fields and ascertaining with greater certainty the changes in the fundus The otologist cooperates by charting the acuity of hearing and by performance of the vestibular reactions (p 2018)

Electroencephalography.—Perhaps the greatest advance in neurological diagnosis has been the introduction of electroencephalography. This method records the electric potentials that originate from the brain and is similar to electrocardiography. The electrodes are placed on the scalp by means

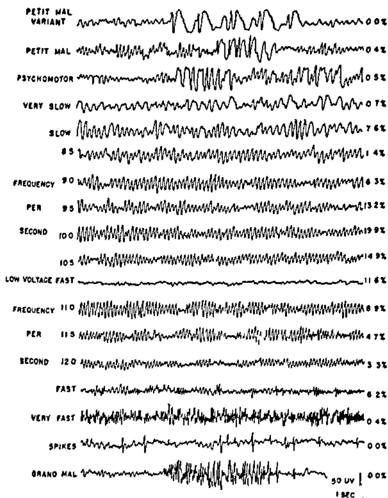


Fig 28.—Types of pattern encountered in electroencephalograms of adults. The order of arrangement is slow at the top, fast at the bottom. The top three and bottom two patterns are classed as paroxysmal, i.e., manifesting seizure discharges. The names applied to each pattern are shown at the left. The percentage incidence of each pattern in the normal control group appears at the right. Time and voltage calibrations are given in the lower right corner.

of collodion. It is rarely necessary even to cut the hair. Through the electrodes the minute scalp currents are amplified by vacuum tubes until they activate an electromagnetic field whose oscillations are noted and written by a pen attached to a sensitive lever.

[illegible] in Manual of Military Neuropsychiatry by Solomon and Yakovlev

The record an *electroencephalogram* is obtained under careful conditions with the patient lying down eyes closed A variety of brain waves" of various amplitudes and frequencies and shapes are observed Among the waves experts identify *alpha beta* and *delta* varieties which vary in frequency and voltage The records of various parts of the skull show differences in voltage and distribution but symmetrical points should give electroencephalograms that are almost identical

The normal electroencephalogram varies with emotional states the solution of mental problems movements of the eyelids sleep and the use of drugs Its greatest value is the altered pattern under pathological conditions such as *idiopathic epilepsy vascular pathology lacerations tumors* of the cerebral tissue and severe *dysfunctions* Localization of tumors of the convexity is made possible in this way

Classification of Electroencephalograms—Many variations are recognized in electroencephalographic tracings The following table based on Fig 258 (p 1403) briefly describes the more important variations with the exception of focal abnormalities which are depicted in Fig 273 (p 1427)

Tracing	*Comment*
Petit mal variant	Seizure discharges present Two per second with alternating wave and spike
Petit mal	Seizure discharges present. Three per second with alternating wave and spike
Psychomotor	Seizure discharges of flat or round topped appearance Record previously free from such activity
Very slow	Less than eight per second Twenty times more common in epilepsy Frequent in organic brain disease especially with convulsions (p 1519)
Slightly slow	Less than eight and one half per second Twice as common in epilepsy
Normal	From eight and one-half to twelve per second. No seizure discharges Normal trace appears in 15 per cent of epileptics
Low voltage fast	Less than 20 microvolts
Slightly fast	Greater than twelve per second Twice as common in epileptics
Very fast	Greater than twelve per second with large amount of activity Twenty times more common in epilepsy and frequent in organic brain disease especially with convulsions
Grand mal	Seizure discharges present Thirty three times more common in epileptics
Focal abnormalities	Abnormal activity in a particular cortical area, indicative of organic brain disease with localization (p 1425)

Reaction Patterns —Involvement of any particular part of the nervous system produces to a greater or lesser degree a specific reaction pattern which is the same whether the area has been traumatized infected infiltrated by neoplastic tissue degenerated or compressed Irritation of *sensory roots* produces neuralgias causalgias and paresthesias while destruction results in loss of sensation On the *motor side* irritations are manifested by fibrillations tremors contractions tics spasms choreiform movements athetosis and convulsions whereas complete destruction is followed by atrophy pareses and paralyses

Localization —The localization of the site of a neurologic lesion is deduced by correlating the abnormalities noted in sensation muscle movement and the reflex arc Lesions that involve a peripheral or spinal *sensory*

nerve are followed by anesthesia without paralysis whereas the contrary situation exists when a peripheral or cranial *motor nerve* is involved

Destruction of a *mixed nerve* is associated with combined motor and sensory phenomena By plotting the cranial or peripheral motor and sensory defects it should be possible to determine whether the pathway has been injured peripherally at the root segmentally in the cord along the pathways or in the supramedullary portions of the nervous system

Neurologic Consultation —Neurologic consultations are provided by the consultant organic neurologist and the neurosurgeon References to the latter are more satisfactory since the decreased morbidity and mortality of operative procedures have greatly widened the scope of surgery and *exploratory craniotomy* and *laminectomy* are often required in the clarification of puzzling neurologic syndromes

NEUROLOGIC THERAPY

Neurologic therapy is far from the confused and hopeless exercise of former times The roster presented below suggests the possibilities of both nonoperative and operative therapeutic measures

Pharmacotherapy —Useful drugs in the treatment of nervous and mental disorders include analgesic antipyretics sedatives and hypnotics anticonvulsants alcohol opiates demerol trichlorethylene cerebral stimulants general anesthetics arsenicals the sulfonamides and penicillin

Other Forms of Therapy —Besides drugs the practitioner may utilize for his neurologic patient the principles of rest restoration of function passive motion active motion exercise corrective exercise occupational therapy the vacation balneotherapy and spa therapy massage lumbar puncture cisternal puncture ventricular puncture intraspinal injection spinal anesthesia caudal anesthesia paravertebral nerve block physiotherapy by heat or cold baths electrotherapy and the electroconvulsive modalities

Specific Nonoperative Therapy

1 Sulfonamides and penicillin in the treatment of meningitis (p 443) and syphilis (p 1377)
2 Ketogenic diets and dehydration in epilepsy (p 1515)
3 Dilantin tridione and phenobarbital in epilepsy ergotamine in migraine (p 1507)
4 Antiluetic therapy in the syphilitic disorders (p 1377)
5 Vitamin administration in deficiency states (p 616)
6 Relief of trigeminal neuralgia by inhalations of trichlorethylene (p 148?)
7 Analgesia with salicylates (p 3833) the coal tars (p 3832) demerol (p 3863) the opiates (p 3853) and cobra venom (p 1049)
8 Treatment of flaccid paralysis by physiotherapy (p 3784)
9 Treatment of spastic paralysis by curare and similar preparations (p 3888)
10 Treatment of respiratory paralysis by the administration of oxygen containing 5 to 7 per cent of carbon dioxide or by a respiratory (Iron Lung)
11 Treatment of medullary paralyses by picrotoxin as in poisoning by the barbiturates (p 3839)

The record, an *electroencephalogram* is obtained under careful conditions with the patient lying down eyes closed A variety of "brain waves" of various amplitudes and frequencies and shapes are observed Among the waves experts identify *alpha beta* and *delta* varieties which vary in frequency and voltage The records of various parts of the skull show differences in voltage and distribution but symmetrical points should give electroencephalograms that are almost identical

The normal electroencephalogram varies with emotional states the solution of *mental* problems movements of the eyelids sleep and the use of drugs Its greatest value is the altered pattern under pathological conditions such as *idiopathic epilepsy vascular pathology lacerations tumors* of the cerebral tissue and severe *dysfunctions* Localization of tumors of the convexity is made possible in this way

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Localization—The localization of the site of a neurologic lesion is deduced by correlating the abnormalities noted in sensation muscle movement and the reflex arc Lesions that involve a peripheral or cranial *sensory*

CHAPTER 69

THE VOLUNTARY NERVOUS SYSTEM CONGENITAL AND HEREDITARY ABNORMALITIES

The majority of congenital anomalies of brain and cord are mere descriptive entities for which treatment holds no promise Spina bifida cranium bifidum and congenital hydrocephalus however present therapeutic potential *in the hands of the expert neurosurgeon*

ANENCEPHALY AND HEMICEPHALY

Absence of the entire brain or half of the cerebrum is incompatible with life The child may survive delivery but succumbs shortly thereafter

PORENCEPHALY

In porencephaly there are small or large unilateral or bilateral defects within the cerebral hemispheres The condition may be the result of defective development although occasionally it follows cerebral hemorrhage trauma or postnatal infection The cavity formations produce marked cerebral atrophy and the child may survive for a few years in an asymptomatic phase as a *mental defective* an *epileptic* or a *paralytic*

Operative Procedures

1 Decompressive craniotomy (p 1429)
2 Decompressive laminectomy (p 1434)
3 Ventriculostomy in hydrocephalus (p 2774)
4 Electrocoagulation of the choroid plexuses in hydrocephalus (p 1409)
5 Operative removal of brain and cord tumors (p 2774)
6 Intraspinal drainage and subarachnoid injection therapy (p 1434)
7 *Intracisternal drainage and therapy (p 3783)*
8 Intraventricular drainage and injection therapy (p 3783)
9 Relief of pain by chordotomy
10 Removal of coccyx for coccydynia (p 3073)
11 Sacral caudal and epicaudal anesthesia (p 3972)
12 Removal of prolapsed nucleus pulposus
13 Division of the scalenus anticus for relief of brachial neuralgias
14 Injections of the sphenopalatine ganglion or the gasserian ganglion in facial neuralgias (p 1482)
15 Resection of the posterior root of the fifth nerve for facial neuralgia (p 1482)
16 Drainage of cerebral spinal cord and meningeal abscesses
17 Removal of epidural and subarachnoid clots
18 Division of adhesions of meninges and of ligamentum flavum
19 Local infiltrations of procaine for trigger points'
20 Neurectomy and neurolysis for peripheral nerve disturbances
21 The surgery of the involuntary nervous system (p *1394*)

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20 Neurectomy and neurolysis for peripheral nerve disturbance
21 The surgery of the involuntary nervous system (p 1394)

CRANIUM BIFIDUM

Cranium bifidum occurs in the infant as a congenital defect in the skull Through this there may be a hernial protrusion of brain (*encephalocele*) or meninges (*meningocele*) The hernial protrusions usually appear in the mid dorsal line they are most common in the occipital region though they may be ventral and extend into the mouth Other associated congenital anomalies include harelip congenital dislocation of the hip club foot and cleft palate



Fig 60—Ventriculograms lateral and anteroposterior showing the huge dilatation of the ventricles in hydrocephalus

At first recognition of the anomaly the practitioner insists upon consultation with the neurosurgeon for *plastic repair* The optimum time for operation is the end of the third or fourth week of life

CONGENITAL HYDROCEPHALUS

Congenital hydrocephalus may be external or internal the latter may be of the obstructive or communicating type and unilateral or bilateral

External Hydrocephalus—External hydrocephalus is more properly regarded as a *subarachnoid accumulation of fluid* In this rare condition the

Reichert, in Christopher Textbook of Surgery

CYCLOPS

The cyclops is a monster with a single medially situated eye and orbit The condition results from a defective development of the anterior cerebral vesicle

MICROCEPHALY

In microcephaly there is a defective development of the whole brain with premature ossification of the skull The microcephalic almost invariably is an *idiot* an *imbecile* or an *epileptic* The surgical approach to therapy by trephining the skull is useless

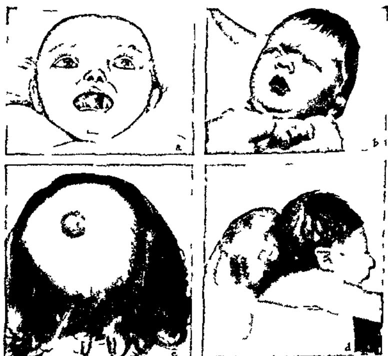


Fig 2_9 —Location of meningoceles *A* Into the mouth through a *cranium bifidum* at the base of the skull *B* Frontal cranium bifidum with meningocele *C* Posterior parietal cranium bifidum with small meningocele *D* Occipital cranium bifidum with encephalomeningocele The nervous tissue was connected with both cerebral hemispheres

CEREBRAL AND CEREBELLAR AGENESIS

Cerebral or *cortical agenesis* which may involve one or both hemispheres produces mental deficiency and cerebral palsies The *cerebellar type of agenesis* is characterized by ataxia and comparatively slight mental defect It may be associated with cerebral agenesis under which circumstance the symptoms of the latter are superimposed Cranial nerve involvements particularly of the facial and ocular nerves may be present *Treatment* is symptomatic

MACROCEPHALY

See *Hydrocephalus* (p 1409)

* Con in Christopher Textbook of Surgery

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Fig 260—Ventriculograms lateral and anteroposterior showing the huge dilatation of the ventricles in hydrocephalus

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Reichert in Christopher Textbook of Surgery

brain fills only a portion of the cranium and the remainder of the cavity is taken up with an excess of cerebrospinal fluid Lumbar puncture reveals an abnormal amount of yellow fluid which flows freely contains a high content of protein and reaccumulates with great rapidity No blockage is demonstrable and dye injected by lumbar puncture appears in the ventricles in appreciable quantities within half an hour

Internal Hydrocephalus—Internal hydrocephalus may be unilateral or bilateral In the *communicating types* of the affliction, there is no blockage *in the ventricular system but the defect is in the absorbing channel*

The *obstructive type* of congenital hydrocephalus is usually due to some congenital defect neoplasm or stricture which blocks one or both



Fig 261 —An extreme case of hydrocephalus This boy age three years had an almost normal mentality *

ventricles Spinal puncture reveals a diminution in the amount of fluid injection of a dye such as neutral phenolphthalein through the fontanelle and into the ventricle fails to produce significant excretion in spinal fluid or urine The ventricular fluid is clear its protein content does not exceed 15 mg and its basal pressure exceeds 50 mm of water

Clinical Manifestations—Congenital hydrocephalus is usually recognized at birth through the enlargement of the head During attempts at delivery it may cause *dystocia* or death of the child The head is large out of proportion to the body the scalp is thin, the veins are prominent the face appears *small and triangular* the eye sockets are widely separated the temples overhang the sutures are wide the fontanelles are tense and pulsating the eyeballs converge the sclerae are visible the child is feeble

* Dandy in Lewis "Practice of Surgery W F Prior Co Publisher

and convulsions occur often Optic atrophy and ocular palsies are observed The child has difficulty in feeding and usually succumbs within a short time Should it survive its development is delayed changes may be observed in the muscles or deep reflexes and intercurrent infection is almost inevitable The skull which has a normal average circumference of 35 to 40 cm at birth may measure 60 to 100 cm On rare occasions positive serological tests for syphilis are demonstrable

Treatment—The hydrocephalic child is referred immediately to the neurosurgeon The external type recognized by the excess of xanthochromic cerebrospinal fluid of high protein content is not responsive to treatment However exploration may be justified on the chance that the condition is a subdural hematoma amenable to surgical therapy

Internal hydrocephalus of the communicating type may be managed by *bipolar endoscopic coagulation of the choroid plexus* This technic requires the services of an experienced expert and should not be attempted unless the mental and physical status of the infant approaches normal Perpetuation of life in an idiotic or hopelessly paralyzed child is not encouraged unless the parents are insistent Many surgeons object to the endoscopic approach since coagulation is effected over the basal ganglia they prefer open operation after application of a plaster cast to the head

In obstructive hydrocephalus an attempt may be made to provide drainage by *ventriculostomy* of the third ventricle Palliative procedures consist of frequent *lumbar taps* in communicating hydrocephalus and repeated *ventricular aspirations* in the obstructive types Congenital syphilitics are given intensive antiluetic therapy (p 2787)

ANOMALIES OF THE CORD

Anomalies of the spinal cord are of rare occurrence They include partial or complete absence *diplomyelia* (splitting of the cord) and *heterotopias* in which the gray matter is displaced in the white substance

None of these disturbances hold any therapeutic possibility and their presence usually is not revealed until postmortem examination

SPINA BIFIDA

Spina bifida (rachischisis) is a developmental defect of the spinal column In the *occulta* variety the bony defect is covered by skin it may be asymptomatic or cause disturbances that are observed only in later life

Spina Bifida Manifesta—Spina bifida manifesta is noted upon the birth of the child as a median line tumor whose usual location is the lower lumbar region Its hernial sac may contain meninges (*meningocele*) or cord tissue (*myelomeningocele*) and the associated neurological manifestations may be mild or severe Other coexistent congenital malformations include hydrocephalus cleft palate harelip or anomalies of the kidney

Clinical Manifestations—The clinical manifestations of spina bifida may be tegumentary or neurologic Often the condition is suspected by the appearance of a dimple a local area of pigmentation or hypertrichosis in the median line overlying the defect The neurological phenomena include incontinence of urine or feces weakness or paralysis of the legs and the appearance of trophic ulcers on the extremities Roentgenograms reveal the defective development of the arches

Treatment—Asymptomatic spina bifida requires no therapy unless the overlying skin is thin and there is danger of rupture and contamination With mild or severe neurologic symptoms operative interference is justified as soon as the infant s condition is stabilized Occasionally exploration reveals divisible bands that have compressed the cauda or a lipoma which can be excised Otherwise the procedure consists of repair of the sac and skin closure

AMAUROTIC FAMILY IDIOCY (TAY SACHS DISEASE)

Amaurotic family idiocy is a congenital malformation in which there is a degeneration of the ganglion cells of the central nervous system revealed by examination of the retina It appears almost exclusively in Jewish children and is fatal within two years or a little more An adolescent

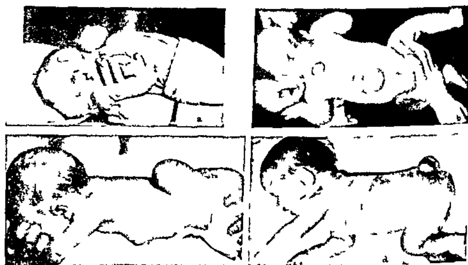


Fig 262—*A* Cervical spina bifida with meningocele *B* Dorsal spina bifida with simple meningocele and lumbar spina bifida with myelomeningocele *C* Lumbar spina bifida with myelomeningocele *D* Sacral spina bifida with meningocele

form occurs in non Jewish children at the ages of seven to eight The pathologic changes suggest that the syndrome is related to Niemann Pick s disease (p 1134)

In its usual form the *clinical manifestations* of amaurotic family idiocy become evident about the fourth or sixth month of life The child which had been developing normally seems no longer able to recognize its mother or its bottle It has difficulty in holding up its head the limbs appear weak and paralyzed and there is sensory hyperacuity as revealed by an excessive response to noise Additional manifestations include nystagmus strabismus and convulsions

The *diagnosis* is established by the ophthalmoscopic finding of the pathognomonic cherry red spot with a surrounding white halo With the progress of time the child deteriorates until it is a vegetating idiot Death usually occurs within the year from intercurrent infection or malnutrition

* Cone in Christopher Textbook of Surgery

NIEMANN PICK S DISEASE

See p 1134

GAUCHER S DISEASE

See p 1133

HAND CHRISTIAN SCHULLER S DISEASE

See p 1137

XANTHOCHROMATOSIS

See p 1135

GARGOYLISM

Gargoylism resembles amaurotic family idiocy (p 1412) except that optic atrophy is not present After the first few months of life the child

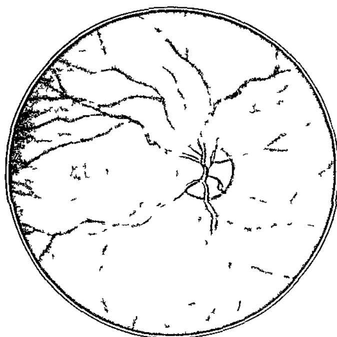


Fig 263—Cherry red spot and opt c atrophy in amaurotic family idiocy and Niemann Pick disea e

appears to be abnormal Vision is defective the arms and legs are short there is a kyphosis the head is large the lips are coarse the eyebrows are bushy the neck is short the abdomen is large and examination reveals an umbilical hernia and enlargements of liver and spleen The child resembles an achondroplastic dwarf and is obviously defective mentally It may sur vive for many years despite retardation

TUBEROUS SCLEROSIS

In its fully developed form tuberous sclerosis is characterized by pro gressive mental deterioration idiocy epilepsy and tumors of the skin and

Courtesy of Drs I Gold tein and D W xler Arch Ophthal Ma 1931

viscera The condition may be mild in its partially developed forms or it may be thoroughly incapacitating



Fig 264 —Sebaceous adenoma in tuberous sclerosis



Fig 265 —Multiple general neurofibromatosis

The characteristic *tegumentary manifestations* include pigmentations and tumors of the skin cafe au lait spots fibromas nevi and *sebaceous*

adenomas (p 3148) over nose and cheeks The *internal visceral lesions* include rhabdomyomas of the heart and fibromas of the intestines and kidneys In rare instances a *phacoma* of the retina is observed The *cerebral changes* consist of nodules of glial tissue which may become transformed into gliomatous tumors resembling glioblastoma multiforme

The *neurologic manifestations* are most often observed in early childhood The infant appears sullen and retarded older children suffer from conduct disorders epileptic convulsions and idiocy The coincidental presence of the dermatological phenomena suggests the diagnosis

Unfortunately the recognition of tuberous sclerosis has only academic importance since there is no available method of therapy that has any promise of benefit Children who are badly handicapped should be institutionalized

MULTIPLE GENERAL NEUROFIBROMATOSIS (VON RECKLINGHAUSEN S DISEASE)

Von Recklinghausen s disease is a congenital and hereditary disturbance characterized by the growth of numerous *fibromas* or *neuromas* The tumors most often grow on sensory nerves of the skin and are accompanied by tegumentary changes in the nature of *pigmented nevi* and *diffuse pigmentations* suggestive of tuberous sclerosis (p 1413)

Multiple neurofibromatosis may present minimal signs or a wide variety of significant clinical manifestations Painful and tender nodules (*tubercula dolorosa*) may require operative removal In *elephantiasis neuromatosa* the tumors are associated with diffuse thickenings of the skin subcutaneous tissues and bones Tumors may grow in awkward positions such as within the spinal canal intracranially or in the cerebellopontine area (p 1426) Very occasionally neoplasms of long duration suddenly develop malignant characteristics

See *Neoplasms of the Cord* (p 1430) *Neoplasms of the Brain* (p 1419)

The *treatment* of von Recklinghausen s disease involves local excision of tumors which are large painful invasive or productive of compression phenomena relative to nearby structures

HEREDITARY SPINAL (FRIEDREICH S) AND CEREBELLAR (MARIE S) ATAXIA

Hereditary ataxia is a chronic familial and progressive degenerative disorder It usually affects several children in a family and is first observed between the ages of six and fifteen The pathological lesion consists of degenerative changes in the posterior and lateral columns pyramidal and spinocerebellar tracts and cerebellum

Friedreich s Spinal Ataxia —The *clinical manifestations* of Friedreich s disease are unmistakable The presenting findings are ataxia weakness of the legs pes cavus equinovarus (clubfoot) scoliosis manus cava nystagmus tremor scanning speech and absent reflexes The dorsum of the foot is high the arch is deeply hollowed and the great toe is hyperextended in the position of a permanent Babinski Sphincteric control is maintained and there are no disturbances in sensation The ataxia being of the cerebellar type is present equally with eyes opened and shut Ocular mani

festations include retinitis pigmentosa juvenile cataracts ocular palsies and atrophies

Marie s Cerebellar Ataxia —The Marie form of cerebellar ataxia represents a variant of Friedreich s disease in which spinal manifestations are minimal

Diagnosis and Treatment —The diagnosis of spinal or cerebellar ataxia is an academic discipline as there is no present method of therapy *Juvenile tabes* (p 1465) is differentiated by the spinal fluid findings *multiple sclerosis* (p 1504) occurs in older patients

FAMILY PERIODIC PARALYSIS

Family periodic paralysis is a rare disease of the nervous system in which there are *attacks of paralysis* of the muscles of trunk and extremities The individual episodes may last for twenty four hours to several days and occur at intervals of a few days to many months The paralysis *usually* comes on at night there are no sensory disturbances the cranial nerves are rarely involved and the paralyzed muscles cannot be stimulated electrically



Fig *66 —Typical foot in Friedreich s ataxia

Hypophosphatemia —The onset of the disturbance is associated with an acute fall in the potassium content of the blood The normal level of 18 to 23 mg per 100 cc may be reduced to 10 mg or less There is a suggestion that the hypophosphatemia is precipitated by the ingestion of a meal that is rich in carbohydrate (p 672)

Treatment —The prevention of attacks of periodic paralysis is accomplished by avoiding high carbohydrate meals and administering 4 to 8 cc of *25 per cent potassium chloride* two to four times daily as needed Ac

* Neurological Service of the Montefiore Hospital

tive therapy consists of the use of hourly doses of 8 cc of the 25 per cent potassium chloride solution until symptoms disappear In extremely severe paralyses involving the respiratory muscles 50 cc of a 2 per cent *potassium chloride solution* may be injected intravenously followed by oral doses in the manner previously described Injections of *adrenal cortical extract* (p 1267) have been suggested through the resemblance of the condition to the acute crises of the Addisonian syndrome (p 1271)

HEREDITARY CHOREA (HUNTINGTON)

Huntington s chorea is a rare hereditary and familial affection in which there is a *chronic progressive chorea* accompanied by *mental deterioration* The disease begins in the fourth decade and is transmitted in direct line through several generations The cause is unknown but the pathologic



Fig 67—Wilson s disease showing associated dental abnormality malocclusion and gingivitis

process which involves the whole brain consists of atrophy of fibers and cells with degeneration of ganglia

Clinical Manifestations—Huntington s chorea begins gradually and first affects only limited parts of the body The *choreic movements* are irregular purposeless and disorderly with facial grimacing a bizarre gait clownish movements clumsy gesticulations dysarthria smacking of the tongue and lips and sudden jerking of the legs The movements are exaggerated by effort tension and emotional stimuli but they disappear at night The *mental deterioration* is initiated by irritability aprosexia impairment of memory apathy suicidal tendencies and progressive impairment to the point of imbecility or total dementia

Course and Treatment—Huntington s chorea runs a progressively unfavorable course and usually requires institutionalization Some symptomatic

festations include retinitis pigmentosa juvenile cataracts ocular palsies and atrophies

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* Neurological Service of the Montefiore Hospital

CHAPTER 70

THE VOLUNTARY NERVOUS SYSTEM NEOPLASMS

Tumors of the Brain
Neoplasms of the Spinal Cord
Neoplasms of the Peripheral Nerves

Neoplastic disease of the voluntary nervous system may involve the brain cord or peripheral nerves Secondary metastases from distant malignancies are of lesser importance to the practitioner than primary tumors Advances in neurosurgical technic have greatly lessened the risks of *craniotomy* and *laminectomy* These procedures should be undertaken whenever there is hope of partial or complete removal of a neoplasm

TUMORS OF THE BRAIN

Tumors of the brain are encountered with great rarity in private practice Nevertheless the physician is required to be on the alert for cerebral neoplasms Institutional experiences reveal unsuspected instances in patients with psychiatric changes of sufficient moment to have warranted commitment to mental hospitals

The nature and incidence of brain tumors are best illustrated by presentation of the chart prepared at the clinic of the late Harvey Cushing (Table 92) The record probably reveals an unusually high percentage of pituitary adenomas through Cushing s particular interest and inordinate skill in the management of these lesions

The Cushing tables reveal that the brain tumors that occur with appreciable frequency are *gliomas pituitary adenomas meningiomas acoustic neurinomas* and *craniopharyngiomas* As the pituitary adenomas (p 11 5) and the craniopharyngiomas (p 117) are elsewhere described the present discussion is limited to a consideration of gliomas meningiomas and acoustic neurinomas

Gliomas—The glioma is the most important and most common brain tumor It is nearly always single often infiltrates the brain and may spread by way of cerebrospinal fluid pathways It is usually surrounded by an area of necrosis and is occasionally the site of *hemorrhage* and *cystic degeneration* Gliomas may be small or so large as to infiltrate a hemisphere

Astrocytomas—Of the classifiable gliomas the commonest are astrocytomas These are *slow growing* capable of removal and somewhat radiosensitive Generally they occur in the *cerebral hemispheres* of adults and the *cerebellar lobes* of children They are somewhat more circumscribed than other gliomas they often calcify and frequently become necrotic or cystic The tumor has comparatively few vessels but many glial fibers and protoplasmic processes (*fibrillary and protoplasmic astrocytomas*) Cerebellar astrocytomas in childhood are particularly amenable to surgical removal the cerebral tumor however can seldom be completely removed

Glioblastomas and Medulloblastomas—The glioblastoma multiforme (*gliosarcoma*) grows rapidly and mainly affects adults of middle age It generally involves the cerebral hemispheres and is subject to cystic or necrotic degeneration *Medulloblastomas* are rapid growing but radiosensitive growths that generally invade the cerebellum in children

Meningiomas (Endothelioma Meningothelioma Ar h o d l o M geal Fibroblastoma)—Meningiomas are the commonest connective tissue tumors of the brain They occur along

relief is afforded by the administration of bromides barbiturates or hyoscine

PROGRESSIVE LENTICULAR DEGENERATION (WILSON)

Wilson s disease is a rare familial condition which affects young people and is associated with a *hobnail cirrhosis of the liver* (p 1969) The af flicted show bilateral rhythmic *athetoid movements* of hands arms legs and face The emotional disturbance is reflected by a *perpetual grin* and *spasmodic laughter* The limbs are spastic and eventually develop contractures, reflexes are active but there is no Babinski sign and no actual weak ness of muscles or loss of sensation abdominal reflexes are preserved speech is dysarthric and there is difficulty in swallowing

The disease progresses inexorably and death occurs within a few years

APLASIA AXIALIS EXTRACORTICALIS CONGENITA (PELIZAEUS-MERZBACHER)

Pelizaeus Merzbacher s disease is a rare congenital and familial abnor mality which begins in infancy The chief clinical features are slowness of speech fixation of facial expression nystagmus ataxia spasticity of the legs and mental deficiency The lesion is an atrophy of the white matter of the brain The course is chronic and uninfluenced by treatment

may also occur *spongioblastomas* which sometimes involve the pons or optic chiasm in children *astroblastomas* *oligodendrogliomas* *ependymomas* which arise in or near the ventricles and tend to calcify *papillomas* of the choroid *sarcomas* which are usually secondary *angiomas* *dermoids* *cholesteatomas* which occur at the base of the brain *osteomas* *osteosarcomas* *enchondromas* *chondrosarcomas* *lipomas* and *metastatic carcinomas*

Clinical Manifestations —The clinical manifestations of the brain tumor may be those of a general increase in *intracranial pressure* or they may be due to *local disturbances* of involved neighboring structures Occasionally *acute degeneration* or *bleeding* gives the symptoms of a non neoplastic cerebral vascular accident (p 1430)

Increased Intracranial Pressure —The generic syndrome of increased intracranial pressure includes headache vomiting dizziness papilledema



Fig 268 —Calcified glioma

convulsions psychic or mental disturbances and alterations in pulse and respiratory rates

HEADACHE AND PERCUSSION TENDERNESS —Headache is often the first sign of brain tumor it may be violent and persistent or relatively mild and paroxysmal it may be diffuse or local and under the latter circumstance it is often accompanied by percussion tenderness of the skull *Localized spontaneous cephalalgia* with corresponding percussion tenderness has some slight diagnostic value but may be most misleading

NAUSEA AND VOMITING —Vomiting is almost universally present in tumors of the posterior fossa (p 1423) It has no relation to meals and may or may not be preceded by nausea Often it is *projectile* probably as the result of irritation of the fourth ventricle or the basal ganglia

DIZZINESS —Dizziness is an important complaint in *infratentorial neoplasms* such as tumors of cerebellum cerebellopontine angle medulla and

the courses of the *meningeal vessels* and the *superior longitudinal sinus* as hard, slow growing vascular neoplasms which invade the dura and produce erosion and thinning or hyperostosis of the overlying skull The tumors grow on the surface of the brain but they do not infiltrate When they become calcified they form *brain sand* and are known as *psammomas* Certain meningiomas tend to recur even if completely removed

TABLE 92—THE NATURE AND INCIDENCE OF BRAIN TUMORS

(From the Clinic of the late Harvey Cushing)

		Number	Percentage
Gliomas		860	43 0
Pituitary Adenomas		3[illegible]8	17 9
Chromophobe	26[illegible]		
Chromophile	8		
Mixed	23		
Meningiomas		26[illegible]	13.2
Neurinomas (acoustic)		170	8 5
Congenital Tumors		111	5 6
Craniopharyngiomas	91		
Cholesteatomas and Dermoids	14		
Chordomas and Teratomas	6		
Metastatic and Invasive Tumors		[illegible]9	3 9
Granulomatous Tumors		47	[illegible] 3
Tuberculomas	3[illegible]		
Syphilomas	15		
Blood vessel Tumors		41	[illegible] 0
Sarcomas (primary)		1[illegible]	0 6
Papillomas (choroid plexus)		11	0 5
Miscellaneous and unclassified		50	[illegible] 5
Total		[illegible]004	100 0

* *Verified gliomas were as follows*

Unclassified			211
Verified by cystic fluid alone		61	
Excluded because differential diagnostic impossible		[illegible]	
Gliomas of optic chiasm		23	
Gliomas of pons and midbrain		2[illegible]	
Atypical gliomas		3[illegible]	
Transitional forms		6	
Classified			649
Neuro-epithelioma		2	
Medulloblastoma		87	
Pinealoma		9	
Ependymoma		23	
Glioblastoma multiforme		196	
Spongioblastoma polare		18	
Oligodendroglioma		27	
Astroblastoma		31	
Astrocytoma		250	
Fibrillary	152		
Protoplasmic	98		
Ganglioneuroma		3	
Total			860

Acoustic Neuromas *(Neurinomas or Neurofibromas (Perineural Fibroblastomas))*.—Acoustic neuromas neurinomas or neurofibromas are encapsulated tumors growing on the eighth nerve They are slow growing and are comparatively easily removed They may be part of a more general neurofibromatosis such as von Recklinghausen's Disease (p 1415)

Miscellaneous Tumors—Besides the common tumors of the Cushing classification there

sciousness suggesting epilepsy facial tics and tonic spasms may be herald manifestations of an intracranial neoplasm The sudden onset of motor irritation in a previously healthy adult is a sufficient indication for a complete survey by the specialist even to the point of exploratory craniotomy

VISCERAL PHENOMENA—With increasing intracranial pressure the *pulse rate* becomes slower and *respirations* may be depressed accelerated or of the Cheyne Stokes type *Hiccough* is a rare symptom but alterations in *temperature* may accompany alterations in pulse and respiratory rates Tumors of the floors of the third and fourth ventricles may produce *glycosuria diabetes insipidus adiposis* and other pituitary manifestations (p 1150)

Localization of Brain Tumors—The localization of the brain tumor is specialist province The diagnostic investigation is approached by clinical examination roentgenography ven-



Fig 2 0—Hyperostosis from meningioma of tuberculum sellae

triculography encephalography spinal fluid examination electroencephalography and exploratory craniotomy

Since the operability of the brain tumor is often dependent upon early diagnosis the practitioner is required to become familiar with localizing symptoms so that the patient may be referred promptly to the neurosurgeon for more elaborate investigation and therapy "Reaction patterns are independent of the nature of the brain tumor whether neoplastic inflammatory or vascular They may be superimposed on the manifestations of *increased intracranial pressure* or they may exist independently

Meningeal Reaction Pattern—Inflammations and hemorrhages involving the meninges are easily recognized through cytologic serologic and chemical changes in the *cerebrospinal fluid* (p 2734) Unfortunately for diagnostic purposes *meningiomas* which usually arise from the arachnoid cells seldom produce such easily recognized manifestations Their presence is suggested by radiographs of the skull which reveal increased *local arterialization* and changes in the density of the overlying bone and by *focal manifestations* which result from pressure on the underlying brain tissue Only late in the course does the meningioma attain sufficient size to cause signs of *increased intracranial pressure* (p 14 1)

Lateral Ventricle Block Reaction Pattern—The paired lateral ventricles lie deep in the brain Their *floor* is made up of thalamic bodies the *lateral walls* are adjacent to the in

pons *Tumors of the fourth ventricle* (p 1424) are characterized by the onset of dizziness with change in position

PAPILLEDEMA —*Choked disk* (*papilledema*) is the *most characteristic single sign* of brain tumor It occurs most commonly when there is blockage of the aqueduct of Sylvius with resultant *internal hydrocephalus* (p 1410) Thus it is almost *constant in* tumors of pineal quadrigeminal plates and posterior fossa it is *also seen in* neoplasms of occipital temporal parietal and frontal regions Unless relieved the choked disk leads to field defects optic atrophy impairment of vision and eventual blindness Tumors that press *directly* on the optic nerve chiasm and tracts may produce as a first sign an *optic atrophy*

PSYCHIC AND EMOTIONAL CHANGES —Psychic and emotional changes are of frequent occurrence Drowsiness yawning clouded consciousness stu

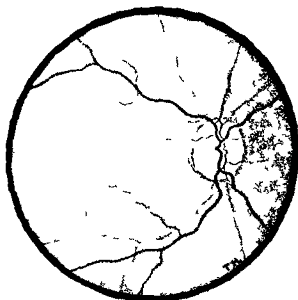


Fig 269 —Simple optic atrophy

por loss of memory personality changes moral defects delusions hallucinations delirium mania facetiousness puerility sexual aberrations and insomnia or somnolence may be encountered Tumors of the third ventricle and pineal often cause hypersomnia personality and sexual aberrations distinguish frontal lobe and thalamic tumors See p 1424

Even highly trained psychiatric staffs have the experience of discovering at postmortem an unsuspected brain tumor in a patient who had been confined as a psychopath This diagnostic error can be avoided only by *suspecting an intracranial growth* in each characterological or psychiatric manifestation of recent or sudden onset Often the diagnosis is clarified only by *exploratory craniotomy*

CONVULSIONS —Convulsions occur most commonly with lesions in or near the motor cortex and the temporosphenoidal lobes *The convulsions may be generalized* or *focal* (p 1519) An attack of petit mal a loss of con

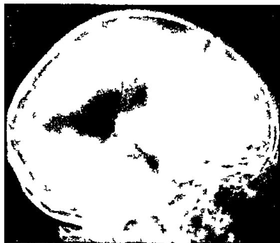
Gifford Textbook of Ophthalmology

Block of the fourth ventricle may occur f om an intrinsic lesion such as an *ependymoma* or a *polar spongioblastoma* The former is not infrequent in adults while the latter occurs in childhood or adolescence Blockage of the fourth ventricle may be intermittent with acute paroxysms of *severe headache nausea vomiti g* and *alterations in pulse and respiratory rates* The attacks often occur with changes in head position

Anterior Fossa React on Pattern—The anterior fossa contains *f ontal lobes* and the *first cranial nerves* The *olfactory nerve sheath* is a not infrequent s te for the origin of a *meningioma* The presenting symptom is *anosmia* followed by the signs of *increased intracranial pressure* (p 1491) Radiographs of the skull reveal th ckening of the bone and increased vascularization

In the *Foster Kennedy* syndrome the anosm a is associate l with ipsilateral optic atrophy and contralateral pap lledema

F ontal Lobe Reaction Pattern—The frontal l bes are the great association and integra t on areas for all funct ons of the nervous system Destruction produces changes in *character* or *personality* manifested by euphoria purposeless jocosity incontinence of urine uneth cal conduct abnormal sexual behavior anxiety regress ons nervousness inattention yawni g fear distractib l ty poor judgm nt and impairme t of memory or intellect *Ab*



F g 9 —Round d defect in th rd ventr le fron te at na of th rd ventricle

no n al movements (grasping and gropin) inab lity to arry out skill d acts (*apraxia*) and py am dal tract dysfunctions occur when the posterior portion of th lobe is destroyed Ad d t onally there may be adrene gic hypothalam c funct ons ncreased contralate al cerebellar gns and symptoms and aphas a

Les ons n the *preroland c area* involving th motor pathways produ e focal irritative o convulsive symptoms (*Jacksonian epilepsy*) Later they lead to contralateral hem plegia w thout sensory s gns until th *post oland c area* n the parietal lobe becomes involved Left ided tumors in right handed pat ents cause motor aphasia

M ddle Fossa React on Pattern—The middle fossa conta ns *parietal occipital* and *temporal lobes sella tu cica pituitary gland optic chiasm optic t acts* and *thi d fourth sixth* a d *fifth cranial ne ves* Pituitary les ons cause erosion of the clino d processes of the sella and enlargement deepen ng and th nning of the pituitary fo s Men ngiomas wh ch usually aris along the vertex or parietal ar a result in th cken ng of the inner layer of the skull and increased vascularization

Parietal Lobe React n P tt rn—The parietal lobe is the great sensory center of the b a n D sturbances produce impairment or abse ce of one or more *cortical sensory modali t e* over the *cont alateral h lf f the body* Th s results in *defect ve sense of body position* with *astereognosis apraxia ncoord nat on and slight weakness* of the affected arm and leg

Peet in Christopher Textbook of Surgery

ternal capsules and the *roof* impinges upon the multiple association fibers between the various centers and the cerebral hemispheres the *temporal horns* are in close relationship to the cortex of temporal lobes and visual pathways

Block of the lateral ventricle is usually *unilateral* and due to a slow growing malignant *ependymoma* The blockage produces manifestations of *internal hydrocephalus* and localizing symptoms which depend upon the pressure upon impinging structures The internal hydrocephalus is recognized by headache nausea vomiting changes in pulse and respiratory rates somnolence and coma Downward invasion adds the *thalamic reaction pattern* (p 1426) *lateral invasion* produces disturbances of the internal capsule with *contralateral hemiparesis* and/or *hemisensory defects and hemianopsia*

An early sign of ventricular displacement is a *shifting of the pineal gland* as seen on lateral or anteroposterior radiographs of the skull when the gland contains enough calcium to cast a shadow More accurate localization is provided by *ventriculography*

Third Ventricle Block Reaction Pattern—The unpaired third ventricle lies between the basal ganglia Its *anterior wall* is adjacent to hypothalamus optic chiasm and pituitary gland the *posterior wall* is in close relationship to pineal gland and secondary nuclei for hearing and vision (corpora quadrigemina) The third ventricle joins the *lateral ventricles*



Fig 971—Ventricular displacement from cystic ependymona The cyst and ventricular system were injected with oxygen independently

by the short foramina of Monro and the *fourth ventricle* by a long narrow iter the aqueduct of Sylvius

Block of the third ventricle is rare and may be caused by an *astrocytoma* or a congenital colloid cyst A lesion of the third ventricle which occludes the *foramen of Monro* produces localized *internal hydrocephalus* of the lateral ventricle as previously described (p 1410)

Occlusion of the iter dilates both lateral ventricles as well as the third ventricle *Posterior dilatation* of the third ventricle displaces posteriorly the pineal gland and through pressure on the corpora quadrigemina causes bilateral impairment of the upward movement of the eyes *Lateral anterior and downward dilatations* give rise to hypothalamic reaction pictures (p 1160) In any event involvements of optic chiasm and/or optic nerves result in bilateral papilledema

Fourth Ventricle Block Reaction Pattern—The fourth ventricle begins at the level of the pons and is located on the roof of pons and medulla The roof of the fourth ventricle itself is thin and lies immediately beneath the mesial portions of both cerebellar hemispheres and the vermis

Peet, in *Christopher* Textbook of Surgery

are resultant difficulties in articulation swallow ng and the rate and regularity of respiration and heart

Pontine Reaction Pattern—Pontine reaction patterns are characterized by *crossed par alyses* which consist of a disturbance of the *ipsilateral cranial nerves* (V VI and VII) and the *contralateral arms and/or legs* pap lledema appears late

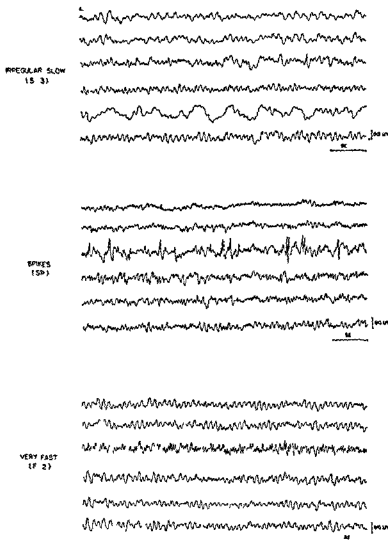


Fig 273—Types of electro-encephalograph c focus that are very reliable ind cators of local d organic bra n damage Time and voltage cal brat ons at the lower r ght in each case

Midbra n React on Pattern—Midbrain reaction patterns are rarely neoplastic The syn dom of *Wernicke s disease* which is probably a vitamin deficiency is elsewhere described (p 1502) A characterist c synd ome (*Weber*) includes ps lateral paralys s of III with con tralateral hem plegia

G bbs in Manual of Mil tary Neuropsychiatry by Solomon and Yakovlev

The patient confuses right and left halves of the body Fairly frequently there is a *homonymous quadrant visual defect* or *hemianopsia* The reflexes on the affected side are variable and may be reduced absent or hyperactive

Temporal Lobe Reaction Pattern—The temporal lobe is the great reception center for hearing equilibration taste smell vision and speech Lesions are characterized by *aphasia* and *defects in the visual field* which are more pronounced when the dominant lobe is affected (left temporal lobe in right handed person) The visual defect is either a *quadrantic or a hemianopic homonymous field defect* apparent on tangent screen examination (p 1643) There may be dream states psychic fits and auditory hallucinations as in the psychoses A *contralateral hemiplegia* with pyramidal weakness may be most marked in the lower face tongue and arms *Uncinate fits* are infrequent but characteristic

Occipital Lobe Reaction Pattern—The occipital lobe is often silent involvement may produce *word blindness* and *homonymous hemianopsia* on tangent screen examination

Pituitary Gland Reaction Pattern—See *Basophile Adenoma* (p 1175) *Cushing's Syndrome* (p 1159) *Acidophile Adenoma* (p 1175) *Pituitary Dwarfism* (p 1161) *Gigantism* (p 1155) *Acromegaly* (p 1156) *Adiposogenital Syndrome* (p 1166) *Simmonds Disease* (p 1169)

Hypothalamic Reaction Pattern—See *Diabetes Inspidius* (p 1180) *Adiposogenital Syndrome* (p 1166)

Pineal Gland Reaction Pattern—See *Macrogenitosomia Praecox* (p 1185) *Cushing's Syndrome* (p 1159)

Thalamic Reaction Pattern—The thalamic reaction pattern is characterized by burning agonizing *intractable pain* over the contralateral half of the body The pain is continuous with acute exacerbations that are initiated by stroking cold emotional stress or strain There may be *ataxia* of the affected arm and leg with associated *abnormal posturing* The hand is cupped with the fingers extended the foot has an accentuation of the arch and the patient walks on the toes There may be contralateral pyramidal tract involvement with *hyperactive* and *pathologic reflexes*

Posterior Fossa Reaction Pattern—The posterior fossa contains brain stem cerebellum basal cisterns and all except the first four cranial nerves The most frequent sites for expanding lesions are cerebellum and cerebellopontine angles

Cerebellar Reaction Patterns—Involvement of a single cerebellar lobe rarely gives symptoms until there has been produced a block of the fourth ventricle the basal cisterns or involvement of the IX XI or XII cranial nerves Early cerebellar symptoms are ipsilateral *incoordination* of the arms and legs unilateral or bilateral *ataxia* with the eyes open or shut *nystagmus* which is slower and of greater amplitude looking toward the side of the lesion and of quicker and lesser amplitude looking contralaterally and slight to moderate rigidity of the neck *Increased intracranial pressure* adds headache nausea, vomiting and papilledema When the *cranial nerves* become involved additional symptoms include corneal areflexia weakness of the tongue palate pharyngeal laryngeal and facial muscles alterations in voice dysphagia, and impairment of facial sensation The reflexes are usually depressed or absent All symptoms and signs are ipsilateral

Bilateral cerebellar involvement is rarely neoplastic and almost always of degenerative origin

Cerebellopontine Angle Reaction Pattern—A common brain tumor is the *acoustic neuroma* which arises from the sheaths of facial or auditory nerves An early manifestation is *unilateral tinnitus* with gradual and progressive *ipsilateral impairment in hearing* there may or may not be attacks of *vertigo* As the neoplasm grows the ipsilateral *face muscle* becomes weakened and then paralyzed in a peripheral manner Examinations reveal *unilateral nerve deafness* with reduction in all responses to *caloric stimulation* (p 2018) A radiograph may show erosions of the internal auditory meatus *Nystagmus* on lateral gaze occurs regularly and early

Later there is reduction in the *pain and temperature senses* of the face especially about the nose and cheeks the *corneal reflex* is absent on the affected side *incoordination* and *ataxia* appear in the ipsilateral arm and leg Finally there are manifestations of *increased intracranial pressure* with nausea, vomiting papilledema and unilateral or bilateral palsy of the sixth nerve Dysarthria, dysphagia and dysphonia suggest involvements of IX and X cranial nerves

Medullary Reaction Pattern—*Tumors of the medulla oblongata produce bilateral signs of pyramidal tract involvement* together with affections of the lowest *cranial nerves* There

are resultant difficulties in articulation swallowing and the rate and regularity of respiration and heart

Pontine Reaction Pattern —Pontine reaction patterns are characterized by "crossed par alyses which consist of a disturbance of the *ipsilateral cranial nerves* (V VI and VII) and the *contralateral arms and/or legs* papilledema appears late

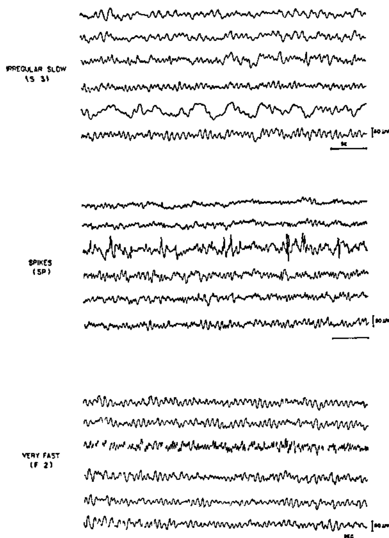


Fig 273.—Types of electro-encephalograph focus that are very reliable nd cators of local ze l org n c bra n lamage Time and voltage calibration at the lower right in each case *

Midbrain Reaction Pattern.—Midbrain react on patterns are rarely neoplastic The syn drome f *Wernicke's disease* which is probably a vitamin deficiency is elsewhere described (p 1002) A *characteristic* syndrome (*Weber*) includes ipsilateral paralyses of III with con tralateral *hemiplegia*

* *Manual of* Military Neuropsychiatry by Solomon and Yakovlev

DIFFERENTIAL DIAGNOSIS OF

Disturbances of the Cerebrum

With definitive disturbance of the cerebrum the practitioner is required to hold consultation with the neurologist psychiatrist and neurosurgeon The problems involved are usually of serious import and the patient is entitled to a specialist opinion

CAUSE	DIAGNOSTIC FEATURES
Congenital and Hereditary Abnormalities	Anencephaly hemicephaly porencephaly cyclops microcephaly cerebral and cerebellar agenesis macrocephaly cranium bifidum and congenital hydrocephalus (p 1409) Obvious defects noted at birth or immediately thereafter
Idiopathic Psychoses	Schizophrenia manic-depressive insanity involutional psychoses and paranoia (p 1373) Normal clinical and laboratory findings
Symptomatic Psychoses	See p 1374 Note presence of definitive etiologic mechanism in history physical examination neurologic status or laboratory data Remember that other neuropathies may coexist.
Neoplasms	Evidences of increased intracranial pressure (p 1421) cranial nerve palsies papilledema headache nausea and vomiting Refer to specialist for electroencephalogram x ray and exploration
Epilepsy	History of convulsive episodes Characteristic encephalogram. Therapeutic response to phenobarbital and dilantin (p 1517)
Hysteria	With approximate but inaccurate imulation of organic neuropathy (p 1353) Negative laboratory findings
Disturbances of Cerebral Hemodynamics	Temporary alterations due to cerebral anemia hyperemia angiospasm or edema (p 706)
Cerebral Arteriosclerosis	Diffuse disturbances associated with other evidences of vascular disease particularly thickening of peripheral vessels narrowing of retinal artery hypertension and nephropathy (p 2362)
Cerebral Vascular Accidents	Acute and ingravescent disturbances resulting from hemorrhage (apoplexy) thrombosis embolization, aneurysmal dilatation and infection of venous sinuses (p 1446) Cautiously obtain spinal fluid and note evidences of bleeding xanthochromia or increased pressure (p 3734)
Trauma to Skull	Cerebral concus ion contusion, laceration or edema may accompany or follow open or closed intracranial injury with or without fracture (p 1450) Look for evidences of cranial nerve involvement and changes in fundus (p 1545) Cautiously obtain spinal fluid (p 3781) Radiography imperative

CON N ED

Meningitides	By extension from skull fracture and nose or ear infections Secondary to bacteremia and generalized infections as in meningococcus meningitis tuberculosis syphilis and pneumococcic invasions Positive findings in cerebrospinal fluid (p 1462)
Nonsuppurative Encephalitides	Particularly in virus diseases (p 449) syphilis (p 1468) tuberculosis (p 1462) rheumatic fever (p 186) and trypanosomiasis (p 531) Positive spinal fluid findings (p 3734)
Suppurative Encephalitides (Brain Abscess)	May occur by continuity from skull fracture or ear and nose infections (p 2128) Metastatic in pulmonary suppuration (p 1469) and amebiasis (p 526)
Encephalopathies	Toxic disturbances of cerebrum usually associated with avitaminoses alcoholism and poisonings or idiosyncrasy to arsenic lead or mercury
Migraine	Idiopathic recurrent headache on familial and constitutional basis Often relieved by ergotamine tartrate (p 1507)
Cranial Mono or Polyneuropathies	Evidences of cranial nerve paralyses with manifestations of disturbances in the brain in its entirety Note motor or sensory defects or derangements in special sensations such as vision, hearing smell or taste

Diagnosis —The diagnosis of brain tumor is the province of the *specialist* The practitioner cannot be expected to carry the investigation beyond the stage of suspicion He notes the symptoms and physical signs seeks evidences of generalized disease particularly syphilis and tuberculosis performs a blood serologic test for syphilis obtains the cerebrospinal fluid (p 3734) and determines the cell count and the protein and sugar concentrations He requests tests for syphilis and the colloidal gold reaction Lymphocytic fluids are examined for tubercle bacilli and injected into guinea pigs The practitioner is warned that lumbar puncture in the presence of papilledema is dangerous

Roentgenography —The specialist continues the examination by taking *radiographs of the skull* These may reveal a shift in the pineal shadow increased local vascularity and enlargement of the diploic veins erosion of the sella changes in the pituitary fossa destruction of the clinoids and erosion of the floor *Ventriculography* and *encephalography* aid in localization The former involves withdrawal of fluid from the ventricles and the introduction of helium or oxygen for contrast radiography The latter is accomplished by doing a lumbar puncture and injecting air into the subarachnoid space with similar intent There seems a general preference for ventriculography rather than encephalography although both procedures are accomplished at a definite risk

Electro encephalography —Electro-encephalography promises more accurate localization of cortical and subcortical growths Characteristic changes found in the waves produced by the electrical current have diagnostic and localization value

Exploratory Craniotomy —There are times when even the expert can

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CONTINUED

tion of the spinal fluid As a result of these multiple possibilities the syndrome of spinal cord tumor is varied and unpredictable The clinical manifestations may be sensory or motor and in either instance may be irritative or paralytic

Pain Rigidity and Percussion Tenderness—Pain and paresthesias are very constant early manifestations of cord tumor particularly when there is involvement of the *posterior roots* Most often the pain is severe and of neuralgic distribution along the involved peripheral nerve The distribution may be unilateral or girdle like At times it simulates *visceral pain* so that exploratory laparotomy is performed for a suspected intraperito-

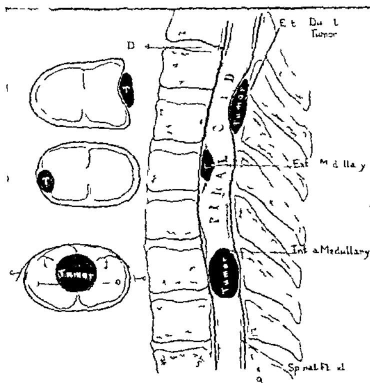


Fig 271—Schematic drawing to show the relation of tumors to the spinal cord and dura

neal disorder (p 1748) Pains in the *lumbar region* (p 2274) are difficult to differentiate from *low back sprains* and *sciaticas* particularly those associated with *herniation of the nucleus pulposus* (p 3074)

The pain of cord tumor is often exaggerated by sneeze cough or straining at stool The overlying spinal muscles are rigid as in arthritis and there may be *localized percussion tenderness* suggesting an osteomyelitis of the vertebral column

Sensory Disturbances—Sooner or later the pain of spinal cord tumor is associated with irritative or anesthetic manifestations Quite characteristically there is often a *band of hyperesthesia* just above the level of the

Stookey in Christopher Textbook of Surgery

neither sustain nor refute the possible diagnosis of brain tumor Under these circumstances it is necessary to do an *exploratory craniotomy* since the operative procedure has little risk and procrastination may cost the opportunity for complete removal of the neoplasm

Brain Abscess—The differential diagnosis of brain abscess (p 1469) is an academic discipline to the practitioner since the inflammatory tumor calls for surgical intervention as surely as a neoplasm

Vascular Disease—Cerebrovascular accidents and *aneurysms of the intracranial vessels* (p 1444) closely simulate expanding tumors especially those in which hemorrhage has occurred A reasonable doubt justifies *exploratory craniotomy* whose commission is a lesser risk to the patient with blood vessel disease than is omission for the person afflicted with the neoplastic disease Cerebral arteriography is of definite value in the recognition of the aneurysm

Treatment—The treatment of brain tumors is surgical As soon as the diagnosis is fairly certain or even suspected an *exploratory craniotomy* is advised by a *specialist neurosurgeon* The tumors that respond most favorably are acoustic neurinomas accessible meningiomas certain pituitary adenomas neurofibromas psammomas and certain gliomatous tumors of the cerebellar hemispheres

Roentgen therapy is indicated for spongioblastoma medulloblastoma glioblastoma astrocytoma pituitary adenomas and all infiltrating tumors

NEOPLASMS OF THE SPINAL CORD

Neoplasms of the spinal cord may be intramedullary or extramedullary The latter occur intradurally and extradurally The most frequent of the spinal cord tumors is the *primary extramedullary meningeal fibroblastoma* This neoplasm arises from the meninges and the sheaths of the nerve roots The more frequent *primary intramedullary tumors* are the *meningiomas* and *perineural fibroblastomas* From the viewpoint of operability it is important to stress the fact that 85 per cent of cord *tumors* are benign and amenable to excision

Secondary implants are usually the result of metastatic carcinoma involving the female breast the stomach the prostate gland or the large intestines

Clinical Manifestations—*Cord tumors occur most commonly* between *the ages of twenty and fifty but they may develop in young* children and the aged The size of the tumor varies from that of a pea to that of a large nut Giant tumors may extend up and down the vertebral canal for a considerable distance hour glass neoplasms grow partly inside and partly outside the spinal canal the waist line being in the intervertebral foramen

The effect of the neoplastic growth is variable and depends upon chance factors Compression of the posterior roots produces early *sensory* manifestations pressure anteriorly involves *motor* areas the cord may be pushed to one side or compressed, the symptoms may result from contrecoup the vascular supply may be cut off leading to secondary cord softening and degeneration the veins may become engorged and varicose the spinal fluid may be blocked with the production of the *Froin Nonne syndrome* of *xanthochromia, increased protein* and *spontaneous coagula*

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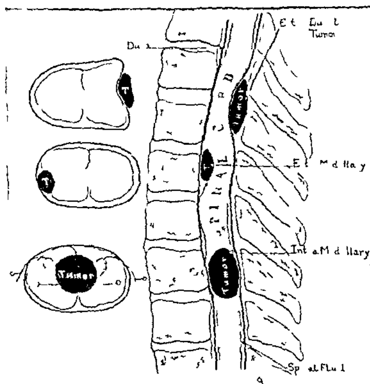


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Hematopoietic	Particularly with hyperchromic macrocytic anemia (pernicious anemia) Note characteristic hemogram (p 1077) and favorable response to liver extract (p 1078)
Pachymeningitis and Arachnitis	Usually secondary to organization of meningeal clots following hemorrhage Simulation of cord tumor discernible only at laminectomy (p 1448)
Myelopathies	Rare metabolic lesion secondary to vitamin deficiency hyperchromic macrocytic anemia or poisoning with carbon monoxide carbon sulfide or chloroform
The Scleroses	Idiopathic lesions of posterior or anterior horns posterior columns or pyramidal tract Diffuse involvement precludes possibility of operative interference Temporal pallor of optic disks in multiple sclerosis (p 1502)
Syringomyelia	Central gliosis with sensory dissociation Contralateral loss of pain and temperature with ipsilateral touch anesthesia (p 1505) Diffuse changes preclude surgical interference

lesion Below this there may be *segmental hypesthesia or anesthesia* A *saddle anesthesia* suggests a lesion of the conus

Involvement of the *spinothalamic tract* gives rise to a *contralateral analgesia* and *thermanalgesia* with resultant burns and *trophic ulcers* produced by heat that had been locally applied for the relief of pain

Motor Disturbances—Pressure of a cord neoplasm on an *anterior root* results in motor weakness followed by atrophy and loss of reflex Should the *pyramidal tract* be involved the limb is spastic deep reflexes are increased the Babinski and confirmatory signs are positive and cremasteric and abdominal reflexes are lost Whether the motor paralysis is flaccid or spastic study of the innervation of the affected muscles assists in determining the tumor level

Visceral Disturbances—Difficulties in urination defecation ejaculation and erection are dependent upon the degree of cord compression and the level of the tumor The initial disturbance is usually a disturbance in *initiating urination* Later there may be *retention* and *overflow incontinence* (p 2265) Difficulties with *defecation* are often early manifestations of compression of the conus Irritative phenomena in the lower cord produce *priapism* but more extensive involvement is followed by *impotence* and *sterility*

Determination of Tumor Level—The practitioner is not required to define with exactitude the level of a cord neoplasm He has fulfilled his purpose if he recognizes the presence of the growth and refers his patient to the neurosurgeon The latter assumes the responsibility of determining the site for his laminectomy and even the expert may be considerably misled by anomalies and contrecoup phenomena

Tumors of the Conus—Tumors of the conus which carry a bad prognosis give early bilateral cord symptoms saddle anesthesia trophic disturbances and marked involvement of the bladder and rectum They are apt to produce symmetrical manifestations with *little pain*

DIFFERENTIAL DIAGNOSIS OF

Disturbances of the Spinal Cord

Disturbances of the spinal cord are complicated by the fact that they may arise secondary to derangements involving the meninges and the osseous and articular structures that make up the vertebral column

CAUSE	DIAGNOSTIC FEATURES
Congenital and Hereditary Abnormalities	Spina bifida Note manifest defect or obtain x ray for occult anomaly (p 1411) Hereditary spinal and cerebellar ataxia (p 1415)
Neoplasms	With pain rigidity and localized percussion tenderness Localizing sensory and motor disturbances Refer to neurosurgeon for x ray laminography spinal manometry and examinations of fluid particularly for xanthochromia (p 3735)
Vertebral Osteopathy	With metastatic carcinomatosis of spine (p 2836) With osteomyelitis usually tuberculous or pyogenic (p 2930) *Note changes in x ray*
Osteoarthrosis	Metabolic disturbance of obese middle-aged Note narrowing of joint spaces and spur formations producing irritations of spinal roots particularly of sciatic distribution (p 2855)
Atrophic Arthritis of the Spine	Generalized arthropathy of young with narrowing of joint spaces and tendency to ankylosis (p 2859) Note rapid sedimentation rate *and peripheral vasomotor disturbances*
Trauma	Lesions secondary to fracture dislocation of spine or transection of cord (transverse myelitis) *History of injury* X ray changes and flaccid or spastic paralyses (p 14∪6) Often associated with disturbances of bladder and rectum
Herniation of Nucleus Pulposus	History of acute chronic or recurrent radiculitis usually of sciatic distribution Defect demonstrable by laminography and laminectomy (p 3704)
Tabes Dorsalis	Syphilitic meningomyelitis with pupillary changes disturbances of deep sensation and characteristic spinal fluid findings Positive serology and decolorization of intermediate tubes in colloidal gold reaction (p 1465)
Acute Anterior Poliomyelitis	Acute virus infection with fever spinal pleocytosis and peripheral nerve palsies usually flaccid (p 4∪7)
Nonsuppurative Meningitides	Most often tuberculous with acid fast bacilli demonstrable in spinal fluid (p 1462) May be of virus origin in lymphocytic choriomeningitis and *equine encephalomyelitis* (p 442)
Suppurative Meningitides	With demonstrable organisms in meningococcal streptococcal, staphylococcal pneumococcal and influenzal invasions (p 1462)

CONTINUED

NEOPLASMS OF THE PERIPHERAL NERVES

The peripheral nerves may be involved in neoplastic processes References are made elsewhere to *acoustic neurinomas* (p 1426) and similar lesions which are often part of a *generalized neurofibromatosis* (von Recklinghausen's disease) (p 1415)

Glomus Tumors—Neoplasms may involve the neuromyo arterial glomus The growths appear as *bluish or purplish nodules* that are most often situated *subungually* Attention is drawn to the lesion by severe and intractable *pain* and exquisite *tenderness* Glomus tumors may appear anywhere in the corium of other parts of the hands and feet

Simple *excision* is followed by immediate relief of symptoms

Tumors of the Cauda Equina—Tumors of the cauda equina which have a more favorable outlook than those that involve the conus are apt to be characterized by *severe pain* retention of bladder and rectal control early loss of knee and ankle jerks and a symmetrical distribution of motor and sensory manifestations

Laboratory Findings—The problem of diagnosis of spinal cord tumor is greatly clarified by radiography manometry and examinations of the spinal fluid

Roentgenography—Upon suspicion of the presence of a cord tumor a *radiograph* of the vertebral column is taken for the possible demonstration of a local lesion which may be responsible for the cord disturbance The frequently encountered abnormalities include fractures and dislocations caries of the spine usually tubercular an osteo arthrosis with spur formation and osteophytes the atrophic type of spondylitis an osteomyelitis a primary or metastatic malignancy or a spina bifida occulta

Queckenstedt s Test—After the radiographs of the vertebral column have been taken a lumbar puncture is performed and *spinal fluid pressure readings* are made with and without compression of the veins in the neck In the recumbent position the normal pressure of the cerebrospinal fluid *is 10 to 15 mm of water Compression of the jugular vein on* both sides of the neck normally is followed by a rise in pressure up to 35 to 50 mm of water Release of the vessels is accompanied by a sharp fall to the previous level When there is obstruction of the subarachnoid space the pressure reactions are absent or delayed

Examination of the Spinal Fluid—At the termination of the manometric readings a *xanthochromic fluid* with an increase of globulin and *spontaneous coagulation* points *to a tumor above the level of the* tap with a fairly complete block of the spinal subarachnoid space The usual examinations are then performed as to cytology albumin and sugar content serology bacteriology and the colloidal gold phenomenon In the presence of a significant lymphocytosis leukocytosis positive serological test for syphilis changes in the colloidal gold reading or a positive growth of a bacterium attention is directed toward conditions other than the spinal cord neoplasm *Contrariwise if all of these tests are negative* but the globulin content is elevated and definitive organic neurological findings are demonstrable the suspicion of cord tumor cannot lightly be dismissed

Treatment—The treatment of the cord tumor is approached through a *laminectomy* and operative removal of the neoplasm if it is at all feasible The expert neurosurgeon is often rewarded by the accomplishment of a complete excision of a meningioma a fibroma a neuroma a neurofibroma and of *certain types of sarcoma*

Inoperable tumors are treated by a *decompressive laminectomy Roentgen therapy* may be of some palliative value in the management of various types of sarcomas intramedullary astrocytomas ependymomas and metastatic lesions Symptomatic surgical therapy for the relief of pain consists of *chordotomy* retention of urine is best managed by a *suprapubic cystostomy* preceded by ligation of the vasa deferentia

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CHAPTER 71

THE VOLUNTARY NERVOUS SYSTEM CIRCULATORY DISTURBANCES

CIRCULATORY disturbances of nervous tissue have the capacity for the production of severe and often irreparable damage Nerve tissue suffers profound change as the result of *local ischemia* from whatever cause *re generation is imperfect if it occurs at all Circulatory disturbances* characterized by hemorrhage and clot formation encroach upon the limited confines of intracranial and intravertebral spaces and result in *compression manifestations* that are identical with those produced by *neoplasms* (p 1419) Traumatic disturbances are elsewhere described (p 1450)

CEREBRAL ANEMIA

Cerebral anemia may be due to systemic or local conditions The *acute anemia of hemorrhage* (p 1057) is characterized by noises in the ears spots before the eyes yawning sighing and syncope Similar symp toms occur in *shock* (p 928) when there is no actual blood loss

The *chronic anemias* (p 1055) are often associated with headache dizziness roaring in the ears loss of memory insomnia drowsiness delu sions hallucinations and headache Extraordinary recovery is the rule when blood volume is restored

Local Cerebral Anemia and Intermittent Claudication—A local cerebral anemia may be due to organic closure of an arterial lumen as described in the paragraphs on thrombosis (p 1123) A similar reaction pattern may be caused by an angiospasm as described in the following paragraphs

Intermittent Claudication—Intermittent claudication of the cerebral vessels may result in transitory aphasia paresis paralysis convulsive twitchings hemianopsia or sensory disturbances These may be *angio neurotic* (p 3349) as well as harbingers of *cerebral arteriosclerosis* (p 1438) *Sensitization to tobacco* (p 3884) may be a factor in isolated instances In the interests of therapy and diagnosis an intravenous injection of

papaverine hydrochloride 32 to 60 mg (½ to 1 grain) is indicated with repetition in 1 to 2 hours

Diagnosis and Treatment —The diagnosis of cerebral angiospasm should not be hazarded until efforts are made to exclude the presence of organic

DIFFERENTIAL DIAGNOSIS OF

Non Traumatic Abnormalities of Cerebral Circulation

See also Traumatic Lesions (p 1450)

	Etiology	Age	Comment
Cerebral Anemia	Blood loss Forward Failure	Any	Relief by correction of etiologic cause
Cerebral Angiospasm	Allergy Tobacco	Young	Intermittent spasms with recurrences on repeated exposure to allergen (p 547)
Cerebral Hyperemia	Backward failure Polycythemia vera Hypertension. Gluttony Sunstroke	Any	Relief by correction of etiologic agent
Cerebral Edema	Head injury Alcoholism Metabolic disturbances such as uremia	Any	Increased intracranial tension relieved by lumbar puncture and intravenous injection of hypertonic sugar
Cerebral Arteriosclerosis	Diffuse vascular disease	After 50	Progressive deterioration
Cerebral Hemorrhage	Cerebral arteriosclerosis	After 50	Acute stroke or shock, usually with hemiplegia
Cerebral Thrombosis	Cerebral arteriosclerosis	After 50	Disability may be ingravescent with slowly progressing manifestations usually hemiplegia
Cerebral Embolization	Pleuropulmonary infection Coronary thrombosis	Any	Sudden onset in patient previously incapacitated by primary disorder
Cerebral Aneurysm	Congenital malformations	20 to 40	May be treated surgically
Subarachnoid Hemorrhage	Arteriosclerosis aneurysm or syphilis	Any	Cerebrospinal fluid bloody or xanthochromic (p 3735)
Thrombosis of the Venous Sinuses	Contiguous infection	Young	May be associated with skull fracture face infection or inflammations of eye ear or nose

disease If the afflicted person is young free from arteriosclerotic change nonsyphilitic with normal intracranial pressure and an otherwise normal neurological status continued conservative observation is warranted An investigation is made for *allergic sensitivities* (p 558) *smoking* is forbidden entirely and forever

CEREBRAL HYPEREMIA

Chronic passive congestion of the cerebral vessels occurs in *backward circulatory failure* (p 941) particularly when associated with *hypertension* and/or *polycythemia* (p 1092) Patients complain of feelings of warmth flushing of the face throbbing in the temples dizziness and headache there may be insomnia injection of the sclerae slowing of the pulse and respiratory irregularities

Active congestion is associated with excitement gluttony bibulousness or with sunstroke It produces pounding in the head dizziness and transitory lapses of memory or consciousness Hyperemic symptoms occur in *acute polycythemia* whether physiological as at high altitudes or pathological as in Osler Vaquez disease (p 1092)

Treatment —Cerebral hyperemia is ordinarily relieved by simple measures such as avoidance of the provocative factors of hyperalimentation and alcoholism A forced *emesis* may be salutary and a *saline purge* produces rapid dehydration The application of *cold compresses* or an ice cap to the skull while the patient is recumbent is often highly effective for symptomatic relief Those who develop symptoms at a high altitude are instructed to take inhalations of *oxygen* until they can return to points nearer sea level

The old remedy of a liberal *blood letting* is still highly to be recommended and may serve prophylactic and psychologic purpose in plethoric high livers

CEREBRAL EDEMA

Cerebral edema or *wet brain* is often associated with *head injury* (p 1450) *alcoholism* (p 3851) and *endogenous intoxications* such as *uremia* (p 2275)

Intracranial pressure may be reduced with rapidity by repeated injections of 50 to 200 cc of 50 per cent *dextrose* or *sucrose* by *lumbar puncture saline catharsis* and a *dehydration diet* (p 664)

CEREBRAL ARTERIOSCLEROSIS

Cerebral arteriosclerosis may be a relatively limited process or a local manifestation of a generalized hardening of the arteries The resultant disturbances are varied and range from minor manifestations to major afflictions such as *cerebral apoplexy* (p 1439) *cerebral thrombosis* (p 1444), the *presenile psychoses* (Pick Alzheimer) or the *senile* and *post apoplectic psychoses* (p 1382)

Autopsies usually reveal much more extensive change than had been suspected by the clinical manifestations the vessels are thick walled and contain arteriosclerotic plaques the convolutions are atrophied the meninges are thickened and the glial substance is increased

Clinical Manifestations —A cerebral arteriosclerosis may be the fundamental lesion responsible for mild dizziness transitory attacks of syncope occasional episodes of nausea and vomiting fleeting paralyses aphasia or dysphonia There may be an *intellectual deterioration* progressing to obvious *dementia* Occasionally the syndrome of *pseudobulbar palsy* is noted with dysarthria difficulty in mastication dysphagia a small step-

page gait emotional instability and drooling *Characterological changes* include irritability excessive or flattened emotions suspicion slovenliness sexual exhibitionalism and senile leering

Rupture of a sclerotic vessel produces the manifestations of an *apoplexy* (p 1439) *thrombotic occlusion* gives a similar clinical picture (p 1444) an *aneurysmal dilatation* may suggest a brain tumor (p 1419) and free bleeding results in *intraventricular* or *subarachnoid hemorrhage* (p 1441) The *senile dementias* are described with the material on psychiatry (p 1382)

Treatment —See *Arteriosclerosis* (p 979)

CEREBRAL HEMORRHAGE (APOPLEXY)

Cerebral hemorrhage or apoplexy results from rupture of a vessel whose wall has undergone local or diffuse pathologic change The damage to the surrounding brain tissue does not differ significantly from that caused by the more frequent *cerebral thrombosis* (p 1444) *cerebral embolization* (p 1444) or bleeding into a *neoplasm* (p 1430) The present discussion may be regarded as applicable to all types of intracerebral vascular accident later material deals with the differences displayed in thrombotic and embolic disturbances

Etiology —The commonest cause for cerebral apoplexy i *arteriosclerosis* of a vessel wall (p 1438) The degenerative process is almost always patchy and may involve the cerebral vessels to greater or lesser degree than those of the general circulation More particularly it may affect a single cerebral artery in a manner disproportionate to the involvement of other intracranial arteries Despite the general contrary opinion cerebral apoplexy is *rarely syphilitic* and most often is associated with *cardiovascular renal disease* and/or *hypertension*

The immediate *precipitants* of an apoplexy may be sudden increases in intracranial tension due to straining at stool excitement coughing vomiting parturition or coitus The syndrome is more frequent in those of the *apoplectic habitus* observed in plethoric individuals who are thickset and short necked (p 3492)

Clinical Manifestations —The apoplectic stroke is often preceded by *premonitory symptoms* such as dizziness headache a sensation of fulness in the head spots before the eyes and anxiety There may be the transitory localizing symptoms of dysarthria muscle weakness aphasia paresthesias vomiting or retinal or sub conjunctival hemorrhages

The Stroke or Shock —The actual stroke or shock sets in suddenly with rapidly developing *coma* and *loss of consciousness* During this period the patient lies limp the face is flushed breathing is stertorous and irregular the pulse rate is slowed the pupils may be dilated but usually react to light corneal sensation is lost deep and superficial reflexes are abolished there may be retention or incontinence of urine and feces the voided urine often contains albumin and sugar and the temperature reading may show an elevation or a hypothermia

Localizing Signs —The *duration* of coma is variable and depends upon the extent of the hemorrhage Sooner or later there appear localizing manifestations such as ballooning of the cheek of the paralyzed side pupil

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peduncles produces the syndrome of Weber with ipsilateral third nerve paralysis and contralateral hemiplegia *Pontine bleedings* are followed by ipsilateral cranial nerve paralysis contralateral limb involvement and crossed anesthesia in which the ipsilateral face and the contralateral body are affected *Bulbar palsies* occur with medullary lesions

Intraventricular Hemorrhage—Intraventricular hemorrhage is characterized by deepening coma pupillary miosis increasing paralysis and rigidity of the involved extremity stiffness of the neck convulsive movements in the limbs generalized decerebrate convulsions a bloody spinal tap marked slowing of pulse and respiratory rates pre agonal hyperthermia and a rapidly fatal termination

Differential Diagnosis—The differential diagnosis of a cerebral hemorrhage during the phase of unconsciousness is discussed with the broader considerations of the management of *coma* (p 1295)

Hemorrhage or Thrombosis—Until the present availability of *anti coagulants* (p 1045) in the therapy of vascular occlusions it was an academic discipline to attempt to differentiate *cerebral hemorrhage* from *cerebral thrombosis* (p 1444) Since the latter condition may be phenomenally alleviated by *heparinization* (p 1050) whereas a bleeding tendency might be seriously augmented by the intended therapeutic measure exact diagnosis now has practical therapeutic importance It is unfortunate that there is no available method of clearly distinguishing cerebral thrombosis from apoplexy However in favor of hemorrhage and opposed to thrombosis are the undernoted clinical phenomena

1 The presence of blood or xanthochromia in the cerebrospinal fluid
2 More sudden onset with headache vomiting or convulsions
3 Rigidity of the neck and the presence of the Kernig sign
4 Unilateral dilatation of a pupil
5 Conjugate deviation of head and eyes
6 A bilateral Babinski reflex
7 Progression of the focal neurological signs
8 A leukocytosis in excess of 12 000 per cubic millimeter
9 A cerebrospinal fluid pressure reading in excess of 350 or 400 mm

Brain Tumor or Abscess—In the stage of paralysis it becomes necessary to consider the possibility that the focal neurologic manifestation originates in a lesion that is operable such as a *brain abscess or neoplasm* (pp 1419 1469) There also remains the eventuality of a coexistence of hemorrhage and neoplasm *since bleeding may occur within a new growth* The existence of a brain tumor or abscess is favored when the patient is relatively young and there are few manifestations of arteriosclerotic disease elsewhere in the body Abatement of the paralytic phenomena argues strongly towards the diagnosis of bleeding persistence or increase in focal signs warrants consultation with the expert neurologist or neurosurgeon who may require *exploratory craniotomy* before a definitive opinion can be established

Prognosis—The prognosis of a cerebral apoplexy is grave but by no means hopeless The majority of the patients survive the accident though few are enabled to resume the normal activities of an average life During

lary contraction in pontine and intraventricular bleedings contralateral abolition of the corneal reflex in supratentorial hemorrhages jacksonian epilepsies conjugate deviations of the head and eyes to the side of the bleeding and away from the paralyzed side obvious weakness of an arm and/or leg or ipsilateral papilledema The superficial abdominal and cremasteric reflexes fail to return on the paralyzed side a Babinski sign is elicited even in the early stages of coma

Stage of Recovery—With minor apoplexies the patient recovers after the lapse of minutes hours or days A fortunate few have no localizin

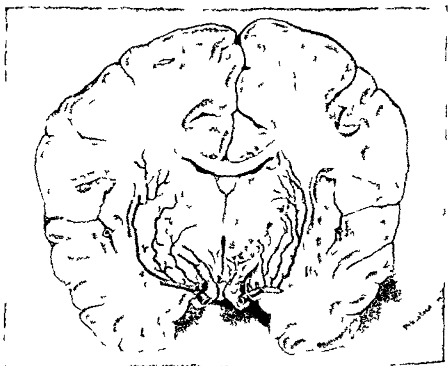


Fig 97a —Diagram showing the branches of the middle cerebral arteries which supply the basal ganglia The innermost are the lenticulo-optic the outer two on each side of the lenticulo striate arteries The outermost of these which pierces the internal capsule to end in the caudate nucleus is known as the artery of cerebral hemorrhage

manifestations but the majority of the afflicted progress to the phase of paralysis

The Stage of Paralysis—The paralytic phenomena that follow cerebral apoplexy depend upon the localization of the hemorrhagic accident Since the involved vessels are most often the lenticulostriate and the lenticulo optic arteries with predominant bleeding into the internal and external capsules there is most often a resultant *hemiplegia* The involved limbs are *flaccid* for several weeks before the *spastic phenomena* of upper cortical neurone involvement become apparent Associated *sensory disturbances* point to a lesion in post central cortical or subcortical areas posterior portion of capsule or thalamus *Hemorrhage into the cerebral*

* MacCallum mod fied from Charcot Duret

nothing to be gained by administering brandy or whiskey or by injections of caffeine camphor epinephrine digitalis strychnine coramine or alpha lobeline The use of sedatives such as chloral bromides opiates and barbiturates is equally ill advised and may cloud significant diagnostic *information Since on rare occasions the hemorrhage may be idiopathic or* a herald manifestation of a tumor consultation with the neurosurgeon merits consideration

Management of the Phase of Paralysis—During the first few days following the accident phlebotomies and intravenous injections of sucrose are repeated according to indication Fluids are administered by rectum or through an intravenous drip urinary secretion is drained off by catheter when necessary No attempt is made to maintain nutrition or disturb the patient by attempts to evacuate the bowels Hypostasis is prevented by turning the patient frequently from side to side The skin is protected by expert nursing which aims at the maintenance of dryness the prevention of soiling and easing of all pressure points

When coma lightens and the patient reacts teaspoonful doses of water are administered Larger amounts are given if swallowing can be accomplished without gagging and coughing The paralyzed extremities are splinted to prevent spastic deformities and contractures

When the patient has thoroughly recovered from the initial shock it is wise to put the joints through their ranges of passive motion These measures have psychotherapeutic value for the patient who is eager to speed convalescence and frets that nothing is being done

As soon as voluntary motion returns the patient is encouraged to focus on active therapy a rubber ball is placed in the hand to aid in the return of strength and dexterity toes and fingers are put through their arcs of motion several times daily *We are of the opinion that electrotherapy* has no beneficial effect and may be harmful in the presence of spasticity

As soon as possible the patient is permitted to sit at the bedside and use a bedside commode Persistent encouragement on the part of the physician is required and *daily visits* are almost a necessity If the physician can think of no other excuse for his continued presence he is justified in giving injections of sodium cacodylate neurophosphates or vitamins in order that *supportive psychotherapy* (p 1316) be sustained *Failure* to make frequent and repeated visits leads the patient to assume that the condition is hopeless and adds the element of despair to the circulatory *accident*

During his visits the physician functions as a *physiotherapist* He conducts resistance exercises in the normal ranges of joint motion and later accompanies his patient on trips to the bathroom the living room down the steps out of the house and to the street If the prophylactic routine (p 1442) has not been instituted before the cerebral accident it is started immediately after recovery in the hope of preventing recurrence

As a rule the apoplectic begins to walk within six to eight weeks and recovery may continue for the period of another year Intelligent and skilful reeducation with a modification of the *way of life* (p 3473) accomplishes much that is good A philosophical patient adjustment may permit a peaceful and comfortable survival for a long period of time

the phase of coma *ominous prognostic signs* include persistence of unconsciousness beyond the first twenty four hours evidences of bleeding into ventricular cavities pons or medulla hypopyrexia or hyperpyrexia bradycardia or tachycardia depression or increase of respiratory rate the onset of Cheyne Stokes respirations a prolonged period of flaccidity of the affected area continued absence of reflexes or an excessively rapid onset of spasticity

Treatment—Prophylactic and symptomatic measures are available in the management of a cerebral apoplexy

Prophylaxis—The prevention of cerebral apoplexy involves the institution of measures employed in the management of *arteriosclerosis* (p 979) *Weight reduction* is mandatory in the obese (p 697) *phlebotomy* is advisable in the plethoric and those who have a polycythemia (p 1092) *moderation* is required in eating and in physical and emotional activities *drinking* and *smoking* are best given up entirely *sedatives* (p 3837) and *hypnotics* (p 3837) are prescribed for tense highstrung individuals the judicious use of *thyroid extract* (p 1189) to aid in weight reduction is suggested in those who have a low basal metabolic rate whether or not there are signs of myxedema social activities are curtailed the amount of work is reduced to that which is absolutely essential for sustenance and the maintenance of self respect

The administration of *iodide* (p 608) accomplishes nothing in our opinion, beyond untoward symptoms *antisyphilitic therapy* (p 340) is reserved for those who are demonstrably luetic and should not be administered on mere pragmatic grounds

The Management of Coma—The immediate treatment of the patient with an apoplexy involves the application of the principle of *skilful neglect* If it is at all possible the patient is not moved or disturbed except for loosening clothes If transportation is required expert handling does much to prevent more excessive damage to delicate nerve tissue

Plethoric individuals benefit by a generous *venesection* (p 3780) intracranial pressure is reduced by *intravenous injections* of 50 to 200 cc of 50 per cent *sucrose* (p 3773) *lumber puncture* is not without danger but is required for diagnostic purposes under which circumstance a minimal quantity of fluid is withdrawn

The application of an *ice cap* to the head can do no harm but probably has little effect other than to give the agitated bystander something to do The bladder region is carefully watched overdistention is prevented by frequent *catheterization* or the temporary use of an *indwelling catheter* Body heat is maintained by blankets but great caution is exercised to prevent burns from awkwardly applied electric pads or hot water bottles Prophylactic therapy with penicillin (p 106) is advised

If there is a suspicion of an angiospastic element an intravenous injection of *papaverine hydrochloride* 30 to 60 mg (½ to 1 grain) is worthy of trial The drug may be repeated within two hours but efforts are best abandoned if two injections fail to cause demonstrable beneficial effects Despite enthusiastic reports we have had no success with the intravenous use of *aminophylline* 0 3 to 0.5 gm (5 to 7½ grains) which has the advantage that it can cause no harm

The apoplectic is often traumatized by overzealous therapy There is

branch to the ipsilateral eye and lies in intimate relationship with the cavernous sinus the third fourth sixth and the ophthalmic divisions of the fifth cranial nerve the sella turcica and the optic chiasm

Clinical Manifestations —The clinical manifestations of the cerebral aneurysm rarely appear before the age period of fifteen to twenty Most commonly they are noted in the third and fourth decades when the aneurysm undergoes dilatation and produces symptoms simulating those of an intracranial neoplasm (p 1419) At this time there may be *bitemporal headache* followed by pressure symptoms resulting from involvement of the surrounding structures Partial or complete *external ophthalmoplegia* suggests pressure on the sixth nerve a *facial neuralgia or anesthesia* is noted with involvement of the first branch of the fifth nerve When the aneurysm is located along the course of the posterior communicating artery an *oculomotor paralysis* becomes manifest enlargement of the sylvian artery as it enters the parenchyma of the brain sets up foci of cortical irritation and *epileptogenic manifestations* erosions into the sphenoid sinus with thrombosis of the cavernous sinus produce an ipsilateral *pulsating exophthalmos* and *papilledema* radiographs may show *erosions of the ipsilateral posterior sphenoid process* and a curvilinear streak just above and lateral to the sella due to calcification within the arterial wall

Sooner or later there is thrombus formation with gradual reduction of the vascular lumen until the carotid is entirely occluded A *slow blockage* may not be associated with clinical manifestations since there is opportunity for the opposite carotid to undergo compensatory enlargement and supply both sides of the circle An *acute occlusion* produces the syndrome of a *cerebral apoplexy* or *thrombosis* (p 1439) Rupture of the aneurysm produces the signs and symptoms of a *subarachnoid hemorrhage*

Treatment —The treatment of intracranial aneurysms involves a *surgical approach* to the internal carotid artery The application of slow compression and eventual ligation of the extracranial portion are the only possible preventive measures for this otherwise fatal condition

SUBARACHNOID HEMORRHAGE

Bleeding into the subarachnoid space results from trauma or rupture of a damaged cerebral vessel weakened as the result of arteriosclerosis syphilitic endarteritis or aneurysmal dilatation

Pathology —In subarachnoid hemorrhage the blood mixes with the cerebrospinal fluid and produces *irritations* of the *cerebral cortex* and the *posterior roots* The extravasated blood clot later serves as a space filling tumor producing the syndromes of *intracranial neoplasms* (p 1419) With complete healing multiple adhesions set up a *pachymeningitis* (p 1448) or an *adhesive arachnitis* (p 1448)

Clinical Manifestations —An intracranial subarachnoid hemorrhage is announced by *vomiting* severe *head pain* followed by *coma* and *collapse* in the manner of a cerebral apoplexy (p 1439) Irritation of the cortex when the blood breaks through the pia may produce *convulsive phenomena* or the patient may display the manifestations of *increased intracranial pressure* (p 14?1)

CEREBRAL THROMBOSIS

Cerebral thrombosis is a more common cause than an apoplexy for the acute intracerebral vascular accident Most often the arterial occlusion is on the basis of an *arteriosclerotic intimal involvement* but it may also occur in the course of an acute illness such as typhoid fever diphtheria or pneumonia it may complicate a surgical procedure or a chronic affliction such as polycythemia vera or the cachexias of malignant disease

Clinical Manifestations—The clinical manifestations of cerebral thrombosis are those of the apoplexy The most striking differential feature is noted in the *ingravescent type* of disturbance in which symptoms are manifest for several days preceding actual loss of consciousness or the onset of paralytic phenomena As in the instance of the cerebral hemorrhage the favored locations are the lenticulostriate or lenticulo optic vessels The clinical phenomena are identical with the exceptions noted in the discussion of the differential diagnosis of cerebral hemorrhage and cerebral thrombosis (p 1441)

Treatment—The course and prognosis of cerebral thrombosis do not differ from those of cerebral apoplexy

Anticoagulants—If the physician can be assured that there is no bleeding and suspects that the vascular occlusion is on a thrombotic basis the use of *anticoagulants* using oral dicoumarol or injections of *heparin* (p 1050) may be attempted for dissolution of the clot and prevention of the spread of the process Because of the dangers involved in heparinization (p 1051) and the present experimental status of therapy this procedure is not advised unless the patient is *institutionalized* and under complete and careful observation It is *contraindicated* if there are obvious evidences of bleeding such as hemorrhagic spinal fluid or xanthochromia (p 3735)

CEREBRAL EMBOLIZATION

Cerebral embolization is a variety of vascular accident that is more apt to occur in young people who suffer from pulmonary and pleural infections and the vegetative types of *endocarditis* (p 1021) In older patients it is observed most commonly following a *coronary thrombosis* (p 983)

Anticoagulants—The presence of the cerebral embolus is suspected when the vascular accident occurs as a complication of the clinical conditions previously listed The recognition of the mechanism of the vascular injury assumes therapeutic importance since *heparinization* (p 1050) may be instituted with the hope of minimizing the damage to brain tissue just as in the instance of cerebral thrombosis (p 1444)

Septic Emboli—Septic emboli may produce abscessed areas in the brain (p 1469) If their presence is suspected *heparinization* is accompanied by the administration of *sulfonamide* or *penicillin* (p 106) for prophylaxis and active treatment

CEREBRAL ANEURYSMS

Cerebral aneurysms occur as *congenital structural malformations* The defect in the vessel wall usually is encountered along the intracranial course of the carotid arteries at their junctions with the anterior portion of the circle of Willis This area of the carotid gives off an ophthalmic

branch to the ipsilateral eye and lies in intimate relationship with the cavernous sinus the third fourth sixth and the ophthalmic divisions of the fifth cranial nerve the sella turcica and the optic chiasm

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The diagnosis is established with certainty if the *spinal fluid* reveals evidence of gross bleeding With the cessation of active hemorrhage the fluid becomes *xanthochromic* the protein content is increased and a *pleocytosis* is observed

Course and Treatment—The course of a subarachnoid hemorrhage is not unlike that of any other type of cerebral accident There may be complete recovery a fatal termination or survival with residual paralyses

Lumbar Puncture—The advisability of performing *lumbar puncture* during the period of active bleeding is seriously debated The advocates are impressed by the reduction of the increased intracranial tension while the opponents fear perpetuation of the bleeding We favor a diagnostic tap The decision regarding repetition depends on the patient s reaction to the first puncture An improvement in symptoms justifies continuation whereas increased difficulties serve as a contraindication Anticoagulants are contraindicated Consultation with the neurosurgeon is imperative

THROMBOSIS OF THE INTRACRANIAL VENOUS SINUSES

The intracranial venous sinuses lie within the dura and receive blood from *intracerebral* and *extracerebral* vessels The most important are the superior longitudinal cavernous and lateral sinuses

Superior Longitudinal Sinus—The superior longitudinal sinus in its most anterior portion connects with the veins of the *nasal cavity* through the foramen cecum In its course between the superior portions of the cerebral hemispheres it receives venous branches from the *skull* and *scalp* and drains venous blood from the neighboring mesial and superior portions of frontal parietal and occipital lobes Posteriorly the superior sinus ends in the lateral sinus usually on the right side

Cavernous Sinus—*The cavernous sinus is located about the lateral* and posterior portions of the *sella turcica* It is formed by the *ophthalmic vessels* and the *angular veins* which drain the nose upper lip cheeks and upper teeth It has no important intracranial branches and unites with the *petrosal sinuses* which communicate with the lateral sinus and the internal jugular veins

Lateral Sinus—The lateral or *transverse sinus* is a paired structure which is located close to the inner ear and makes connections with the veins of the *mastoid bone* the *middle and internal ear* It also receives branches from the closely situated petrous bone and the lateral portions of the temporal lobe The paired lateral sinuses empty into the jugular veins by way of the sigmoid sinuses

Etiology—*Primary thrombosis* of a venous sinus is very rare and when present, is a component of the late stage of cachexia in the young or old

The most frequent cause of thrombosis of the venous sinuses is *infection* resulting from an inflammatory process in a nearby structure The commonest lesion is a *phlebitis* which arises in the extracranial areas and spreads to the communicating intracerebral veins and venous lakes The *secondary thromboses* cause venous occlusion and intracerebral disturbances such as edema perivascular inflammation encephalitis diffuse cortical and subcortical lymphocytic infiltration encephalomalacia multiple petechial hemorrhages or brain abscess The pathological changes may remain *localized* or involve an entire cerebral hemisphere

Clinical Manifestations —The clinical picture of intracranial sinus thrombosis consists of systemic symptoms and localizing manifestations that vary with the site of the involvement

Systemic Symptoms —The generic manifestations of septic endophlebitis include *chilling a hectic fever leukocytosis bacteremia petechial hemorrhages enlargement of the spleen* and *metastatic deposits in the lungs* Unless there is an associated meningitis the spinal fluid is clear and sterile a *lymphocytosis* suggests an impending subarachnoid involvement (*meningitis sympathica*) and positive cultures or a polymorphonucleosis point to an actual break in the meningeal barrier

Superior Longitudinal Sinus Thrombosis —Thrombosis of the superior longitudinal sinus is uncommon and its presence is usually masked by the signs and symptoms of the primary intracerebral lesion such as an abscess hemorrhage or neoplasm Less often it follows infections of the scalp or skull particularly in enfeebled infants

Locally there is *tenderness* over the vertex and an associated *edema* which may spread downward over the forehead The frontal and temporal veins are usually dilated the patient complains of *headache epistaxis nausea* and *vomiting* the associated encephalitis produces *lethargy drowsiness* or *convulsions* the *fontanelle* of the infant may bulge

Since the superior longitudinal sinus lies between the paracentral lobules of the brain which are the cortical centers for bladder control there is usually *incontinence of urine* Involvement of the motor and sensory cortex may produce *weakness or paralysis of one or both lower extremities* with or without impairment of the cortical sensory modalities in the lower extremities Other neurological signs and symptoms depend upon the location of the underlying intracerebral pathology The course of the affliction is rapidly downhill with death in a few days or weeks

Cavernous Sinus Thrombosis —The reaction pattern resulting from thrombosis of the cavernous sinus is fairly constant and usually follows an acute infection in the butterfly area of the face

The venous circulation of the orbit and face are impaired producing *periorbital edema chemosis proptosis congestion* and *dilatation* of the frontal and retinal veins and *papilledema* There may be relatively few associated symptoms but *headache diplopia nausea* and *vomiting* accompany the more severe infections Peripheral involvement of the cranial nerves III IV VI and the first branch of V produces partial or complete *internal or external ophthalmoplegia* impairment of the primary sensory modalities over the *forehead* and *corneal anesthesia* The signs and symptoms are ipsilateral unless the thrombosis spreads to the opposite cavernous sinus

Lateral Sinus Thrombosis —The lateral sinus is more frequently involved than the other venous sinuses because of the high incidence of *ear infections* (p 2145) Uncomplicated thrombosis of the lateral sinus produces *edema* and *tenderness* over the *mastoid area* with congestion and thickening of the peri auricular and jugular veins Infection of the thrombosed sinus brings about secondary infection of the brain or meninges with signs of *encephalitis brain abscess* or an *otogenic meningitis* (p 2148) Papilledema is a late sign

Gradenigo Syndrome —The Gradenigo syndrome consists of a palsy of

the external rectus (VI) and symptoms referable to the sensory division of V These structures are caught up with an inflammatory process near the apex of the petrous portion of the temporal bone (*petrositis*)

Treatment —The prognosis and treatment of sinus thrombosis have been altered by the introduction of the anti-infective agents *Prophylactic chemotherapy* has reduced the incidence of these previously ominous complications to the point where they are now clinical rarities *active therapy* has all but abolished the necessity for performing formidable surgical procedures The addition of *anticoagulants* (p 1050) to the chemotherapeutic efforts holds even greater promise of effectual control

In the pre sulfonamide era there seemed no therapeutic approach to the problems of thromboses of the superior longitudinal and cavernous sinuses The operative treatment of thrombosis of the lateral sinus consisted in exenteration of the mastoid cells evacuation of the infected clot and ligation of the internal jugular veins The superimposition of an otogenic meningitis robbed the patient of any chance for recovery but even this complication responds extraordinarily well to intensive chemotherapy with sulfonamides (p 88) streptomycin (p 103) or penicillin (p 106)

ANEMIA OF THE CORD

There may be a rapid development of *paralysis* after profound systemic hemorrhage The suggested explanation is a resulting anemia of the spinal cord *Intermittent claudication* of spinal vessels with temporary level phenomena have also been described

ARTERIOSCLEROSIS OF THE CORD

Sclerotic changes of the vessels of the cord have been observed with secondary degeneration of the posterior and lateral columns and scattered lesions in white and gray matter These phenomena are difficult of diagnosis and must occur with great rarity

MENINGEAL HEMORRHAGE

Meningeal hemorrhages may be *epidural* or *subdural* They may produce immediate signs or manifestations due to the presence of the clotted blood or cicatrix

Meningeal Subarachnoid Hemorrhage —Subarachnoid bleeding follows trauma to the cord obstetric injuries convulsions hemorrhagic diathese spinal cord tumors or rupture of an aneurysm at the base of the brain (p 1444)

Subarachnoid hemorrhage in the region of the spinal cord is characterized by sharp *pain in the back* and symptoms *referable to the nerve roots* There may be *muscle spasm* from irritation or *paralyses* of the arm or leg The course and prognosis vary with the cause of the disturbance

Symptomatic relief is afforded by *lumbar puncture* which is not without risk and is not to be repeated if followed by evidences of more extensive damage

Pachymeningitis Interna Hemorrhagica and Adhesive Arachnitis —Organization of the meningeal clot leads to pachymeningitis interna hemorrhagica This affliction may give the manifestations of a *cord tumor* (p 1430) with compression phenomena (p 1433) The hemorrhage also may termi

nate in a *circumscribed serous meningitis* or an *adhesive arachnitis* whose symptoms and signs are those of a spinal cord neoplasm (p 1430)

Laminectomy and division of the adhesions or the evacuation of loculated fluid may clarify the entire clinical disturbance *Roentgen therapy* is said to be of additional value

OCCLUSION OF A SPINAL ARTERY

Occlusion of a spinal artery may result from cord tumors arteriosclerosis with thrombosis syphilitic endarteritis or embolization in the course of a septicemia

Spinal Cord Circulation—In the cervical region anterior and posterior spinal arteries arise from the vertebral arteries The *anterior spinal artery* is unpaired and has no anastomoses until it reaches the fifth cervical segment Below this level it is formed by the union of the lateral spinal arteries which arise from the intercostal and lumbar arteries The latter enter the spine along with the anterior roots The anterior spinal arteries on entering the cord give off lateral twigs which supply practically all of the spinal cord except the posterior columns

The posterior spinal arteries are two in number and run along the posterior surface of the cord They receive no anastomoses until the fifth cervical segment Below this level they are formed by the union of lateral spinal arteries that come also from the intercostal and lumbar arteries The posterior spinal arteries enter the spinal cord and supply the area of the posterior columns The *lateral spinal arteries* give off numerous anastomoses which supply and penetrate the whole periphery of the spinal cord

Clinical Manifestations—Compression of a lateral twig of the anterior spinal artery can produce an almost complete *Brown Sequard reaction pattern* (p 1476) except for the posterior column signs Severe compression of the anterior spinal artery before it branches may produce the syndrome of a *complete transection of the cord* (p 1457) except for retention of posterior column function Compression of the posterior spinal artery excludes both posterior columns (p 1476) leaving intact the remainder of cord function Compression of the peripheral anastomotic network of blood vessels may produce focal areas of necrosis in the periphery of the cord

Treatment—Thrombotic occlusions may be treated tentatively by *heparinization* as in cerebral thrombosis (p 1050)

HEMATOMYELIA

Hemorrhage into the spinal cord may be spontaneous or it may occur from trauma (p 1450) cord tumors syringomyelia and blood dyscrasias (p 1085) The hemorrhage is primarily into the gray matter of the cord and often spreads up and down in the gray column Bleeding into the cord substance is destructive and may produce manifestations of partial or complete transection of the cord (p 1457)

Clinical Manifestations and Treatment—The outstanding signs and symptoms of hematomyelia are sudden focal *segmental pain and weakness* The cervical cord is most frequently involved with sudden pain in the shoulder or arm flaccid weakness of the hand and arm and segmental sensory signs of a syringomyelic type (p 1505) As a rule recovery is spontaneous and fairly complete over a period of six months although a high cervical hemorrhage is often fatal Treatment is symptomatic

CHAPTER 72

THE VOLUNTARY NERVOUS SYSTEM TRAUMA AND MECHANICAL DISTURBANCES

The delicate nerve tissues of the brain and cord are well protected by the meningeal coverings the water bed' of the cerebrospinal fluid and the bony structure of the skull and vertebral column Significant injuries do not often occur but when they are encountered they have grave implica tions The practitioner who first sees the injuries to the nervous system is required promptly to recognize the extent of the trauma and exercise skilful judgment in the management of the situation until the expert neurosurgeon can be consulted Whether the injury involves brain or cord the first requirement is *protection against further damage* resulting from injudicious handling or overzealous attempts of therapy Later the con trol of *shock* (p 928) is attempted and efforts are made to reduce *increased pressure relationships* within the skull or column

HEAD INJURIES

Injury to the brain and its coverings may or may not be associated with fracture of the skull The latter in point of fact is of slight impor tance relative to the significance of damage to the underlying tissue The practitioner must not be too greatly impressed with positive radiological evidence nor should he be lulled into a sense of false security by a "nega tive report

SKULL FRACTURES

Skull fractures may be simple or compound linear depressed or pene trating

Linear Fracture —The simple linear break is most frequently seen and may be relatively unimportant though roentgenologically most impres sive Most linear fractures occur at the *base* of the skull When the line of fracture crosses the middle fossa with rupture of the dura and ear drum bleeding occurs from one or both ears The fracture is then *com pound* and carries the danger of *otogenic meningeal infection* (p 2148) If only the dura is torn the drum reveals a collection of blood clots in the middle ear, *paracentesis* at this time is ill advised Rupture of the dura also becomes obvious through *blackening of both eyes* or the escape of spinal fluid through the nose (*cerebrospinal rhinorrhea*) In the latter in stance bacterial invasion of the meninges is invited through a *rhinogenic pathway* (p 2128)

Treatment —The uncomplicated linear fracture of the skull of itself requires no treatment beyond a period of careful observation for at least two to three weeks Compound fractures in which the meninges are exposed through the scalp nose or ear require intensive and immediate *prophylactic anti infective therapy* with *sulfonamides* (p 88) and/or *penicillin* (p 106) and *consultation* with the neurosurgeon With a *rhinorrhea* lumbar puncture is strictly avoided The temptation to evacuate blood clots from the middle ear also must be resisted

Depressed and Penetrating Fractures —Depressed fractures of the skull are often compound and usually lacerate the meninges or brain tissue The depressed fracture irrespective of the intracranial complications (p 1452) requires immediate *consultation* with the neurosurgeon who may deem it advisable to elevate the fragment as soon as the condition of the patient permits

Penetrating fractures produce laceration of the meninges and brain with the introduction of various foreign and infective material They require *surgical attention* as well as *supportive anti infective therapy* using the sulfonamides (p 88) and/or penicillin (p 106)

INTRACRANIAL INJURIES

Following a head injury the damages to the brain may or may not be related to the bony fracture The pathological manifestation may be limited to a *cerebral edema* (p 1451) with petechial hemorrhages or there may occur gross *contusion* or *laceration* (p 1452) with hemorrhagic phenomena such as *epidural subdural subarachnoid* and *subcortical bleedings* Superimposed on the manifestations due to anatomical changes are the syndromes of *shock* (p 928) and *increased intracranial pressure* (p 1421) Late sequels due to organization of clots include *pachymeningitis* (p 1448) *arachnitis* (p 1448) *encephalomalacia* and *cerebral atrophy*

CONCUSSION

Concussion is best illustrated by the knockout blow of the prize ring The pugilist momentarily *loses consciousness* and falls to the floor He is limp with dilated pupils apnea and an imperceptible pulse In less time than it takes to count ten he may rise to his feet and continue the bout but it is observed then that his coordination is poor his timing of blows loses its keenness and the knees seem to buckle After a complete knock out the patient may awaken with *headache* and may have an *amnesia* for the span of time that elapsed between the receipt of the blow and the awakening the head is dulled dizziness is observed and an attempt to rise to the feet is often associated with stumbling

Amazing recovery may supervene so that the defeated fighter makes his way to his dressing room takes off his clothes showers and dresses for the street without apparent ill effects On the morning after he may observe post concussive manifestations such as dullness headache dizziness nausea vomiting and mental retardation but experienced fighters in perfect condition maintain that there are no ill effects

Treatment —The ringside treatment of the knockout consists of sponging the face with water and the inhalation of *smelling salts* It would seem

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advisable to *compress the abdomen* at this time but experienced trainers and seconds prefer to loosen the tights and suspensories

The practitioner in the course of his routine duties rarely observes a brain concussion since the patient has already recovered by the time that he arrives It is his duty then, both from the standpoint of medical and medicolegal implications to insist upon an *observation period* of at least several days Accuracy of observation usually is seriously impaired by the administration of drugs particularly sedatives hypnotics and opiates as well as by the well intended efforts of bystanders who ply the victim with an alcoholic drink

A *radiograph of the skull* is mandatory since basilar linear fractures occur much more often and much more insidiously than is generally believed Furthermore at the time of the injury the attendant has no way of knowing whether or not the recovery represents a mere *free interval* to be followed by *deepening coma* (p 1295) within the course of the next several hours or days

In the home it should be possible to obtain hourly counts of the *respiratory and pulse rates* and four hourly rectal *temperature* readings Institutional observation requires additional estimations of systolic and diastolic *blood pressures* *Lumbar puncture* is postponed unless there are definitive localizing neurologic manifestations or evidences of increased intracranial pressure A neurosurgical consultation is imperative

The period of observation should be no less than seven to ten days if all is well This principle undoubtedly errs on the side of conservatism but it is far better to overtreat many patients than to be negligent of a single one at a price of chronic incapacitation and invalidism

CEREBRAL CONTUSION AND LACERATION

The transition from the syndrome of concussion to the phases of contusion and compression is difficult of recognition Under the latter circumstances the period of unconsciousness is prolonged the patient lies curled on one side and movement of the head is associated with sudden *explosive vomiting* Intense swelling of the brain and the exudation of lymph and blood elevate intracranial over venous pressure the cerebral veins collapse cerebral tissue becomes congested and the medullary centers suffer from ischemia Evidences of *increased intracranial pressure* (p 1471) are noted *respirations* slow and become irregular or of the Cheyne-Stokes variety a progressive *bradycardia* is observed in association with elevation of *systolic* and *pulse pressure* fluctuations in *temperature* from 1 to 8 degrees are noted in the absence of infection With *complete collapse* the blood pressure falls the pulse races breathing slows and the patient displays hyperpyrexia and manifestations of cardiac failure Mentally the patient varies between coma and restlessness there is frequent vomiting severe headache urinary and fecal incontinence or retention and a confusing leukocytosis Neurosurgical consultation is imperative

CRANIAL NERVE COMPLICATIONS

Together with the nonspecific factors of shock concussion and increased intracranial pressure a head injury may be accompanied by localizing symptoms referable to the cranial nerves *Anosmia* (I) is associated with

fractures which traverse the anterior fossa in the region of the cribriform plates The *eye grounds* (II) reveal important evidences of the extent of intracranial damage A retinal hyperemia occurs early with increasing engorgement a *papilledema* appears particularly in chronic subdural hematomas (p 1454) injury to the optic nerve is associated with *blindness* impingement on the chiasm produces a *bitemporal hemianopsia* When III IV or VI are involved the patient notes *diplopia* The sixth nerve is most frequently affected in basal fractures associated with hemorrhage Oculomotor paralysis (III) produces *external strabismus ptosis* and *dilatation of the pupils*

A tear of the infra orbital branches of V produces *anesthesia* along the nose and upper lip the upper teeth are involved when the dental branches are caught Injury to VII results in complete or incomplete *facial paralysis* and lesions of the auditory nerves (VIII) are revealed by *diminution in hearing* and *disturbances in equilibrium* The ninth tenth eleventh and twelfth nerves are well protected and are seldom damaged in head injuries

Treatment —The patient who has passed beyond the phase of concussion requires a *lumbar puncture* for purposes of diagnosis and therapy The presence of fresh blood indicates a subarachnoid hemorrhage (p 1445) clear fluid under increased pressure suggests edema or bleeding into brain tissues which do not communicate with the subarachnoid space

The suspicion of cerebral contusion or compression constitutes an urgent indication for *specialist consultation* Meanwhile the *conservative therapy* outlined in the management of concussion (p 1451) is continued but the practitioner errs if he fails to share the responsibility of the situation with his consultant

EPIDURAL HEMORRHAGE AND BLEEDING OF THE MIDDLE MENINGEAL ARTERY

A linear fracture which crosses the meningeal groove in the temporal bone may produce an epidural hemorrhage from a tear of the *middle meningeal artery* Under these circumstances a characteristic history is elicited *The patient* recovers consciousness and later lapses into *coma* The free interval varies from minutes to hours and may last several days It is characterized by *headache* and *tenderness* on the side of the injury There is often *contralateral motor weakness* due to the clot the first evidences are usually in the facial muscles and the pupil of the affected side usually is dilated

Signs of *increased intracranial pressure* (p 1421) accompany the second period of unconsciousness In contrast to concussion epidural hemorrhages are associated with *increased reflexes* on the contralateral side and positive pathological reflexes such as the *Babinski* The *spinal fluid* is under increased pressure and does not reveal blood unless there is additional oozing into the subarachnoid space *Surgical intervention* at this time with removal of the clot and control of bleeding may produce a phenomenally successful result

SUBDURAL HEMORRHAGE

Subdural hemorrhage results when the meningeal vessels are torn on the under surface of the dura The free interval may or may not be ob-

served the manifestations and treatment are similar to those of epidural hemorrhage (p 1453)

CHRONIC SUBDURAL HEMATOMA (PACHYMENINGITIS HEMORRHAGICA INTERNA TRAUMATICA)

The chronic subdural hematoma may follow a seemingly trivial blow The progress of the hemorrhage is so insidious that symptoms may not appear for weeks or months *Headache nausea vomiting disturbances in vision papilledema restlessness negativism* and *untidiness* are noted These often are interpreted as evidences of *traumatic neurosis* (p 1356) but this diagnosis cannot be maintained in the presence of localizing signs such as Jacksonian *convulsions changes in the reflexes alterations in the visual fields increased spinal fluid pressure* or *xanthochromia*

As in the instance of the epidural hemorrhage the chronic subdural collections are amenable to *surgical therapy*

SUBDURAL HYGROMA

After head injuries the ruptured arachnoid membrane may permit the cerebrospinal fluid to escape into the subdural space The material is not absorbed and forms a foreign body similar to the subdural hematoma (p 1454) The findings are identical until exploration has been accomplished

SUBARACHNOID HEMORRHAGE

Subarachnoid hemorrhage which is the result of trauma may be so extensive as to cover most of a cerebral hemisphere The blood seeps down over the cord and the spinal fluid reveals evidences of fresh bleeding

The symptoms and signs of subarachnoid hemorrhage from trauma are identical with those that occur from rupture of an arte iosclerotic vessel (p 1438) or an aneurysm (p 1444) The patient has *severe headache* and may be in complete *collapse* Stiffness of the neck on flexion a positive Kernig sign leukocytosis bloody spinal fluid and occasional localizing symptoms are observed

The problems of *therapy* particularly referable to the advisability of lumbar puncture are elsewhere discussed (p 1446)

SUBCORTICAL HEMORRHAGE

Subcortical hemorrhages usually occur at the juncture of gray and white matter If they involve the motor area or the internal capsule they may produce a *contralateral alternating hemiplegia* In the midbrain or brain stem they result in the characteristic picture of a *decerebrate rigidity* the entire body is stiff the arms are extended and rotated inward the wrists are flexed the legs are rigid and extended with pronation of the feet (slipper position) *Treatment* is expectant

TRAUMATIC PNEUMOCEPHALUS

Following trauma to the skull a communication may be established between one of the paranasal or mastoid sinuses and the cranial cavity A portal of entrance is created which permits air to enter the ventricles subarachnoid or subdural spaces or even penetrate into brain substance The condition is suspected when the patient notes *violent headaches* fol

lowing coughing sneezing or blowing of the nose A cerebrospinal rhinorrhea is frequently present Roentgenograms clearly depict the condition which requires prompt and intensive *chemotherapy* often followed by *operative interference*

POSTTRAUMATIC DISTURBANCES

Following the head injury a variety of persistent symptoms may be encountered At times these are continuations of the original complaint but again they may not arise for several weeks or months The principal features are vague disturbances such as headaches dizziness weakness irritability changes in memory and disposition insomnia or anxiety Less often localizing phenomena are seen such as posttraumatic epilepsy with Jacksonian attacks evidences of compression of cranial nerves (p 1480) or the features of a pachymeningitis hemorrhagica interna (p 1454)

The posttraumatic sequels are usually suspected of being of functional origin as in a *traumatic or litigious neurosis* (p 1356) The differential diagnosis is most difficult but the presence of any organic finding in the physical examination or any positive manifestation in the spinal fluid requires the practitioner to abandon any thought that the complaints are on anything other than a real and tangible basis *Specialist consultation* is mandatory since medicolegal complications are the rule rather than the exception

ARTERIOVENOUS ANEURYSM

With fracture of the *sphenoids* an abnormal opening may be established between the wall of the *internal carotid artery* and the *cavernous sinus* The back flow results in *stabbing pain* centered behind the affected eyeball the production of a *pulsating exophthalmos* with an *audible bruit* dilatation of the veins of the upper lid forehead and temple papilledema engorgement of the scleral vessels and disturbances in vision

Specialist consultation is required to consider the possibility of gradual occlusion of the involved carotid

BIRTH PALSIES (LITTLE S DISEASE CEREBRAL DIPLEGIA INFANTILE CEREBRAL PARALYSIS CEREBROCEREBELLAR DIPLEGIA AND INFANTILE SPASTIC HEMIPLEGIA)

The birth or cerebral palsies are probably due to injury of brain tissue as the result of *parturition* Some may be the result of infantile disturbances in *blood coagulation cerebral hypoplasia* or *degeneration* but the end results do not differ

Clinical Manifestations—The usual clinical manifestation of cerebral palsy is *spastic diplegia* or Little s disease The infant is observed to hold its legs in adduction As the child begins to walk the gait appears jerky the youngster walks on his toes the thighs are adducted the knees rub together and the legs cross (*scissors gait*) Similar changes may be observed in the arms The deep reflexes are lively the Babinski and confirmatory signs are elicited and the abdominal and cremasteric reflexes are generally absent The spastic diplegia often is associated with imbecility epileptic or Jacksonian convulsions cranial nerve palsies (p 1480) dysarthria abnormal involuntary and associated movements of a choreo athetotic variety

On suspicion of a cerebral palsy, the *neurosurgeon* is summoned and spinal fluid examination is indicated With a bloody tap surgical exploration is considered since later procedures hold little promise

Treatment —Many spastic paraplegics make remarkable accommodations to their affliction With patience, muscle reeducation and the execution of orthopedic procedures the handicapped child may lead a useful and reasonably complete existence Best results are obtained in institutions which have specially trained staffs

There has been some recent encouragement from the use of intocostrin a preparation allied to *curare* for the relief of spasm An intramuscular dose of 1 cc per 20 lbs of body weight but not to exceed 4 cc is followed in a few hours by amazing relaxation which may last two or three days after which another injection may be given See p 3888

INJURY TO THE SPINAL CORD

Injuries to the spinal cord may or may not be associated with damage to the vertebrae As in the instance of head injury there may be concussion contusion penetration or compression of the cord with or without bleeding into the meninges

SPINAL CONCUSSION OR SHOCK

Spinal concussion is as genuine a clinical entity as concussion of the brain (p 1451) The syndrome follows jarring injuries with or without a solution of continuity In all likelihood the local pathologic lesion consist of a focal edema of the cord with punctate hemorrhages

Clinical Manifestations —In spinal shock there is loss of motor sensory and reflex action but maintenance of the control of the sphincters Spinal shock may be marked by a clearly delineated *level* as in spinal cord tumors (p 1433) The *zone of anesthesia* may be surmounted by a *girdle of hyperesthesia* The paralyzed limbs are *flaccid* and may remain inert for ten days to two weeks At the end of this time a phase of *reflex hyperexcitability* may be encountered, a Babinski sign is elicited the thigh and knee are flexed the ankle is extended and trophic changes may appear in the skin with the formation of decubitus ulcers

The terminal phase of spinal shock is that of *diminished reflex excitability* with retention of urine secondary bladder infection and an ascending uropathy (p 2334) Bedsores appear and the paralyzed muscles exhibit atrophy and wasting

Treatment —The management of spinal cord shock calls for *expert consultation* Overzealous therapy may inflict irreparable damage and operative interference holds little promise The management of the *cord bladder* is the most urgent problem and is elsewhere discussed (p 2331)

CONTUSIONS AND LACERATIONS OF THE CORD

The clinical manifestations of contusion and laceration of the cord differ very little from those of cord concussion There may be more clearly defined localization of the injury and the finding of blood in the cerebrospinal fluid The differentiation is of academic importance since little can be done by way of therapy

CORD COMPRESSION

Cord compression may be the result of the direct impingement of a neoplasm a blood clot or a fracture dislocation the encroachment upon the intravertebral space of edema inflammatory exudate or a vascular swelling

The symptoms and signs of cord compression are described elsewhere (p 1430) If the symptoms warrant *laminectomy* is advisable for diagnostic and therapeutic purposes If the mechanisms producing the compression cannot be removed a decompression is accomplished

TRANSECTION OF THE CORD

Transection of the cord may result from trauma or inflammation (*transverse myelitis*) In either instance identical manifestations are noted

Clinical Manifestations—Spinal cord transection results in a *flaccid paralysis* below the level of the lesion muscle tone is lost the limbs are cold and cyanotic there is absence of reflexes and sensation the sphincters of the bladder and rectum are paralyzed As the result of involvement of the tracts of the involuntary nervous system there is usually a temporary drop in blood pressure which may last from twelve to twenty four hours

In the beginning transection of the cord does not differ in its manifestations from *spinal concussion* (p 1456) However at the end of three weeks few changes are noted in the organic findings the phase of hyperexcitability is not observed and there is no return of sensation or muscle power

Treatment—The spinal cord transection is a serious lesion Particular care is required in transportation if the injury is thoracolumbar the *patient is best carried prone on a well-padded litter* with cervical lesions the patient is carried supine Skeletal traction with tongs applied to the skull may be tried in the effort to reduce cervical fractures

Surgery—As soon as the patient is hospitalized specialist consultation is required to discuss the feasibility of performing a *closed reduction* of a fracture or dislocation or a *palliative laminectomy* over the level of the lesion The urgency of a decision is emphasized by the fact that failure to relieve existing pressure on the cord within eighteen hours is followed by permanent damage

While there is considerable difference of opinion concerning operative procedure most surgeons agree that laminectomy is indicated only when the neurological signs are progressive The operation should not be performed merely because there is radiographic evidence of bone pressure or the demonstration of a partial or complete block by the Queckenstedt test (p 1434)

Conservative Therapy—The later conservative management of cord transection requires unusual medical and nursing skill The treatment of the *paralyzed bladder* is a subject of considerable difference of opinion Tidal drainage can be used for weeks but in permanent lesions it is necessary to do a suprapubic cystostomy with prophylactic and continuous *chemotherapy* using the sulfonamides Repeated catheterizations and the use of an indwelling catheter invite infection and augment the difficulties of medical care Later in the course of the affliction the cystostomy tube

may be clamped off and the patient makes effort at voluntary urination employing compression in the hypogastric region If this is successful the tube is withdrawn

The problem of *defecation* is best managed by a daily enema or irrigation *Hypostatic pneumonitis* is avoided by frequent changes in position and the effects of the sulfonamide drugs used for the urinary tract condition A *cradle* is placed over the lower limbs which are *splinted* to prevent deformities from foot drop *Light massage* is not objectionable *Re educational exercises* under expert tutelage, are advised for the limbs as soon as motor activity begins to return Pressure points are protected by padding and the frequent application of talcum powder After the initial lumbar puncture for diagnostic purposes further drainages of cerebrospinal fluid are hazardous

HEMORRHAGIC LESIONS OF THE SPINAL MENINGES

As in the instance of the cranial meninges the spinal cord coverings may become irritated or compressed by fluid or clotted blood A *subdural hematoma* acts in the manner of a *spinal cord neoplasm* (p 1430) Organization of the clot produces the manifestations of a *pachymeningitis interna hemorrhagica* (p 1454) or a *diffuse arachnitis* (p 1448) These manifestations become apparent only upon *exploratory laminectomy* Under these circumstances simple removal of the abnormal tissue or division of adhesions may result in the relief of the clinical abnormalities

FRACTURES AND DISLOCATIONS OF THE SPINE

Fractures and dislocations of the spine assume importance only in so far as they affect the underlying meninges or nerve tissues *Compression fractures* result from *indirect violence* transmitted through the feet head or shoulders or by sudden marked extension or flexion of the body as in an accident or a therapeutically induced *convulsion* (p 1330) The fracture may be primary or secondary to a malignant metastatic or a chronic inflammatory granuloma

Fracture dislocations of the spine involve a break of the body of the vertebra or its processes and associated dislocation of the transverse processes This injury in addition to compression of the spinal root causes *cord compression* and vascular disturbances leading to a *hematomyelia* (p 1457) It requires specialist consultation

INJURIES TO THE PERIPHERAL NERVES

Injuries to the peripheral nerves assume great importance since their effects which may be devastating are amenable to prompt and competent nerve surgery

Etiology—The peripheral nerves of the extremities are particularly vulnerable to traumatic disturbances They may be severed or crushed by direct injury with gunshot or stabbing they may become involved in dislocations and fractures they may be caught up in a callus formation or suffer injury from the pressure of a cast or bandage they may suffer compression from trauma in sleep under anesthesia during a prolonged intravenous injection or as the result of an awkward position during a surgical procedure they may be squeezed or stretched by a neon or

an osteo arthrotic spur they are crushed by the pressure of the scalenus anticus with or without the presence of a cervical rib they may be injured at birth or by spinal caudal or epicaudal anesthesia through accidental injection into the nerve or through the toxemia of a systemic disease such as diphtheria botulism or leprosy

Clinical Manifestations —Injury to a peripheral nerve is associated with phenomena of irritation or paralysis The former causes *paresthesias cau salgia* (p 1476) and *neuralgia* (p 1490) With paralysis there is loss of touch temperature pain and deep sensibility in the area supplied

Motor irritations result in spasms tics and fibrillations while *paralysis* produces a reaction of degeneration to electrical stimulation with loss of reflex loss of strength flaccidity and diminution in volume Trophic vasomotor and secretory changes accompany peripheral nerve injuries The skin becomes glossy and smooth changes are noted in sweating and the appearance of the nails and hair ulcerations are prone to develop *and persist*

The localization of the injured peripheral nerve is discussed in greater detail in the charts that accompany the discussion of the *peripheral mono neuropathies* (p 1490)

Treatment —The establishment of a definitive peripheral nerve lesion is an urgent indication for *specialist consultation* The specialist with great dexterity is often enabled to accomplish *primary or secondary suture* Im mediate repair is favored unless there are evidences of infection or contami nation in the near vicinity Other useful operative procedures include *neu rolysis* in which the nerve is dissected free from scar tissue and placed in a new bed division of the scalenus anticus removal of the nucleus pul posus or excision of a neoplasm

CHAPTER 73

THE VOLUNTARY NERVOUS SYSTEM INFECTIONS

BACTERIAL infections of the voluntary nervous system usually represent secondary localizations following systemic invasions With demonstrable organisms such as the meningococcus an *initial bacteremia* is recognized and this phase may or may not be followed by a meningeal reaction In the instance of the more frequent virus infections the sequence of events is not capable of proof but may be deduced from the clinical course in which the neurologic phenomena follow the systemic manifestations

The *tissue reactions* to infection are a variable *Coccal invasions* are associated with suppuration but most other reactions are concerned with lymphocytic and fixed tissue cell responses Infrequently, the structures are damaged by *circulating toxins* but most often the disturbance results from the presence of *bacterial bodies*

ELECTIVE LOCALIZATION OF NEUROLOGIC INFECTION

The majority of bacterial invaders exhibit *specific affinities* for constituent portions of the voluntary nervous system The exceptions are the organisms responsible for *syphilis* and *tuberculosis* The former variously attacks the brain (*general paresis*) cord (*tabes dorsalis*) meninges or blood vessels (*meningovascular lues*) and may additionally react by *gumma formation* in any conceivable site The tubercle bacillus has the potential for the production of *meningitis* (p 1462) *miliary tubercles* or *tuberculomas*

With these exceptions the bacterial invaders of the voluntary nervous system appear to be more discriminating in their localizations The toxins of *diphtheria* and *tetanus* specifically attack the *peripheral nerves* and the *myoneural junctions*, the viruses of *zoster* and *acute anterior poliomyelitis* localize in peripheral nerves or the cord the *pyogens* set up *purulent meningitis* (p 1462) and the majority of the *encephalitides* result from viral infections

NONSUPPURATIVE ENCEPHALOMYELOMENINGITIDES

Nonsuppurative infections of the brain cord peripheral nerves and meninges without exception are local manifestations of systemic invasions

Etiology—Of the roster of living invaders listed in the table of Elective

Localization of Infection in Nerve Tissue (p 1462) only coccal invaders and *H influenzae* produce suppurative inflammation The remaining cocci bacilli spirochetes viruses and protozoa evoke a lymphocytic or fixed cell response

Clinical Manifestations—The clinical manifestations of the non sup purative encephalomyelomeningitides are considered in the Section de voted to the Infections (p 442) The three notable exceptions are tabes dorsalis meningovascular syphilis and tuberculous meningitis which for

TABLE 93—INFECTIONS INVOLVING THE SPINAL CORD AND PERIPHERAL NERVES

Specific Infection	Clinical Characteristics	Diagnostic Criteria
Diphtheria (p 309)	Membranous inflammation of naso-pharynx with secondary peripheral neuritis often bulbar in distribution	Culture of local mem brane specific anti toxin therapy
Tetanus (p 294)	Infected wound with secondary toxemia sensitizing myoneural junctions and causing tetanic and convulsive phe-nomena	Culture of wound spe-cific antitoxin therapy
Leprosy (p 273)	Peripheral thickening of nerves espe-cially ulna with anesthetic nodules	Stains of nasopharyngeal secretion for organism
Syphilis (p 331)	Gumma of cord rarely seen manifesta tions of cord tumor with positive serology	Blood and spinal fluid serology positive ther apeutic response to iodide
	Tabes dorsalis (locomotor ataxia) (see p 1464)	Blood and spinal fluid serology tabetic gold curve
Herpes Zoster (p 435)	Shingles vesicles and pain along course of peripheral nerve	Clinical appearance
Acute Anterior Poliomyelitis (p 457)	Generalized infection with secondary flaccid paralysis of bulbar regions or extremities ascending paralysis (Landry)	History of endemic el ar spinal fluid with nor mal sugar content early polymorphonuclear pleocytosis followed by lymphocytosis
Pyogenic Organisms	Cord abscesses causing reaction pat-tern of cord neoplasm (see p 1480)	Operative findings

purposes of convenience are presented despite the inconsistency in the present chapter

Differential Diagnosis—The differential diagnosis of the nonsuppurative encephalomyelomeningitides has been presented elsewhere in tabular form (p 449) Main reliance is placed upon epidemiology the clinical history and the more objective information gleaned from examinations of the cerebrospinal fluid and of the serum for virus neutralizing bodies and for fixation of complement

Treatment—The treatment of nonsuppurative inflammation of nerve tissue is a most disappointing experience Exceptions to this generality are

happily found in the prevention of rabies and in anti syphilitic measures in tabes dorsalis

TUBERCULOUS MENINGITIS

Tuberculous meningitis is usually a terminal manifestation of an acute miliary tuberculosis in childhood and infancy In older individuals or adults, contamination of cerebrospinal fluid may occur long after the hematogenous seeding and may appear as the only active manifestation of a tuberculous infection

TABLE 94—INFECTIONS INVOLVING THE MENINGES

Specific Infection	Clinical Characteristics	Diagnostic Criteria
Staphylococcic Meningitis Streptococcic Meningitis	Secondary to compound skull fracture otogenic (p 2148) or rhinogenic (p 2128)	Purulent fluid with gram positive cocci
Pneumococcic Meningitis	As above but also may be secondary to bacteremia	Purulent fluid, with gram-positive cocci
Meningococcus Meningitis (p 213)	Meningeal reaction pattern with acute or chronic bacteremia	Purulent fluid with gram negative cocci
Influenzal Meningitis (p 286)	Meningeal reaction pattern following respiratory infection or bacteremia	Purulent fluid with gram negative bacillus
Tuberculous Meningitis (p 1462)	Meningeal reaction pattern usually in tuberculous children Choroid tubercles often seen	Clear lymphocytic spinal fluid with coagulum containing acid fast bacilli
Syphilis (p 1468)	Meningovascular type produces meningeal reaction pattern in luetic	Positive serology in blood and clear spinal fluid good response to anti luetic treatment
Epidemic Parotitis (p 483)	Meningeal reaction pattern following mumps	Clear lymphocytic fluid
Lymphocytic Choriomeningitis (p 448)	Meningeal reaction pattern following grippal attack	Clear or ground glass spinal fluid with mono nucleosis Virus neutralizing bodies appear later

Clinical Manifestations—Tuberculous meningitis may start insidiously or acutely In the infant it is noted that the child has become irritable constipated and drowsy appetite fails and food is vomited seemingly without cause At first the temperature variations may be mild and variable but later fever increases until the terminal hyperpyrexia With progression of the lesion the fontanelle bulges drowsiness proceeds to the point of stupor convulsions are interpolated and evidences of increased intracranial pressure become manifest The retinal veins appear full the pulse rate alternates between bradycardia and tachycardia and the respira

TABLE 9.—INFECTIONS INVOLVING THE BRAIN

Specific Infection	Clinical Characteristics	Diagnostic Criteria
Rheumatic Fever (p 190)	Chorea	Clinical sequence
Pertussis (p 2 8)	Encephalopathy after whooping cough	Clinical sequence
Tuberculosis (p 252)	Tuberculoma simulating brain tumor (p 1419)	Other evidences of tuberculosis or operative findings
Brucellosis	May produce encephalitis or meningitis (p 314)	Isolation of organism or positive skin test
Syphilis (p 331)	Gumma simulates brain tumor (p 1419)	Response to iodide
	Meningovascular lues	Positive serology and response to antiluetic therapy
	General paresis (p 13)	Positive serology paretic gold curve
Measles (p 409)	Encephalitis (p 44) after eruptive disease	Clinical sequence
Rubella (p 41)	Encephalitis (p 449) after German measles	Clinical sequence
Varicella (p 4 0)	Encephalitis (p 44) after chickenpox	Clinical sequence
Variola (p 4 4)	Encephalitis (p 44) after smallpox	Clinical sequence
Vaccinia (p 4 8)	Encephalitis (p 44) after vaccination	Clinical sequence
Epidemic Encephalitis (p 441)	Multiple involvements in epidemic form	Clear spinal fluid with moderate lymphocytosis
St Louis Encephalitis (p 454)	As above	Virus neutralizing bodies in convalescence
Equine Encephalomyelitis (p 4 1)	Cerebral and cord involvements	Ground glass fluid with lymphocytosis and virus neutralizing bodies in convalescence
Japanese B Encephalitis (p 415)	Probably corresponds to American types of encephalitis	
Russian Seasonal Encephalitis	Probably corresponds to American types of encephalitis	
Rabies (p 439)	Hydrophobia following bite	Examination of brain of bitten animal
Torulosis (p 496)	Encephalitis or meningeal reaction pattern	Torula in spinal fluid
Amebiasis (p 523)	Brain abscess in dysentery patient	Ameba in stool or abscess pus
Trypanosomiasis (p 531)	African sleeping sickness	Organisms in blood smears

tory rate may slow speed or become totally irregular Older patients com plain of headache and changes in personality are noted

Physical examination reveals the bulging fontanelle in infancy stiffness of the neck opisthotonos positive Kernig and Brudzinski signs and finally the choroidal tubercle reveals itself by ophthalmoscopy

Laboratory Findings —The finding of tubercle bacilli in the cerebrospinal fluid leaves no doubt as to the diagnosis of tuberculous meningitis The fluid is under increased pressure and may appear clear or somewhat hazy The globulin content is increased but sugar and chloride contents are re duced The cell count is elevated to several hundred primarily lympho cytes If the fluid is permitted to stand over night a pellicle forms When this is picked out and stained by the carbolfuchsin method (p 52)

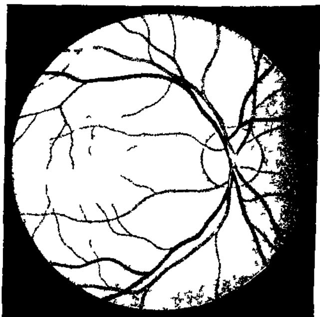


Fig 276 —Miliary tuberculosis of the choroid The yellowish gray color of the spots is due to edema and opacity of the overlying retina (Koellner)

acid fast organisms can be demonstrated without exception if the search is conducted with patience for several hours

Treatment —Tuberculous meningitis is a universally fatal disease despite all efforts and heroic therapy If the physician is impelled to employ meas ures of desperation he may try massive doses of streptomycin intrave nously and intrathecally (p 106) in association with promin used orally (p 267)

TABES DORSALIS (LOCOMOTOR ATAXIA)

Tabes dorsalis represents a *syphilitic infection* in which there is a dif fuse and bilateral involvement of the *posterior horn cell group* with pri mary or secondary degeneration of the *posterior columns* Additionally there may be lesions of the *ascending spinal cerebellar pathways* and the cranial nerves particularly II III IV and VI

Clinical Manifestations—The initial symptoms of tabes dorsalis consist of *painful dysesthesias* from irritations of the affected posterior roots With impairment of the centers for vibration position and deep pressure the patient is disoriented relative to his position in space and notes difficulty while walking *in the dark* or *sways when he covers his face with his* hands while washing Examination at this time reveals a *loss of vibratory sense* a *positive Romberg test* diminution or complete *loss of deep re flexes* in the knee and ankle regions *absence of pain sense* on compression of the Achilles tendon or the testes and *patches of anesthesia* along the lateral sides of the calf thigh or foot

Ocular Disturbances—Almost without exception there are accompany ing ocular manifestations The *pupils* are irregular in size and shape and unequal (*anisocoria*) the light reflex is lost but the power of accommoda tion is retained (*Argyll Robertson pupil*) There may be weaknesses or paralyses of the external ocular muscles and a *primary optic atrophy*

Locomotor Ataxia—As the sensory manifestations progress the patient reaches the ataxic stage where he is unable to walk with any degree of steadiness Characteristic gait changes appear in which the foot is raised high off the ground wavers unsteadily and then is flapped noisily to the floor The mechanical damage produced by this method of locomotion leads to the formation of the *Charcot joint* (p 2953) The weight bearing struc tures of the hip knee ankle and spine are most often involved in a *painless deforming arthropathy* with such complete destruction of the joint structures that the end stage is a bag of bones

Tabetic Crises—The most horrible of the tabetic symptoms are the crises which may be *peripheral* or *visceral* Agonizing lightning pains occur in the muscles of the extremities abdomen or chest They are described by the patient as burning gnawing lancinating twitching or resembling a stabbing with a hot knife The attacks come on with the rapidity of lightning they may last for several hours or days with brief intervals of freedom Other associated abnormal phenomena include paresthesias numbness sensations of cold warmth and tingling

The visceral crises give rise to many difficulties in diagnosis They may be *gastric salivary lacrimal rectal vesical laryngeal pharyngeal* or *sexual* The most frequent is the *gastric crisis* characterized by recurrent abdominal distress vomiting and pain resembling an organic *intra abdom inal affliction* (p 3555) the referred phenomena of a *coronary occlusion* (p 983) or an *angina pectoris* (p 890)

Disorders of the Sphincters—The progression of the tabetic process eventually leads to involvement of the sphincters of the bladder and rectum Either *incontinence* or *retention* may be observed Under the lat ter circumstance the bladder eventually becomes distended with the re sultant introduction of infection and the possibility of an *ascending urin ary sepsis* (p 2334) An early complaint is *dribbling* with difficulties in the initiation of the urinary stream and a feeling of incomplete emptying after micturition At the time of sphincteric involvement *sexual debility* and eventual *impotence* are almost invariable though the latter may occur despite the integrity of the mechanisms of urination and defecation

Trophic Disturbances—Local trophic disturbances occur in the nature of *atrophies* and *penetrating ulcers* Particularly in those with gastric cri

ses and disturbances of bladder function a *generalized cachexia* develops *progressively and the patient loses weight and strength in the manner of* one suffering from a carcinomatosis (p 572)

Laboratory Findings —The laboratory findings in tabes dorsalis may be confirmatory or wholly confusing If they are characteristic the fluid is clear, there may be up to 100 *lymphocytes* in the cell count blood and spinal fluid *serologic reactions* are positive, the *colloidal gold test* shows little or no change in the first two tubes moderate alteration in the third fourth fifth, sixth and *seventh tubes and a normal appearance* thereafter Such a reading might be 0123332100

In the *early stages of syphilis* primary as well as secondary it is not unusual to obtain the laboratory findings that are characteristic of a tabes without any confirmatory clinical manifestations Asymptomatic cerebro spinal syphilis is much more important of recognition than the fully developed tabetic syndrome since therapy, at this time holds great promise of cure' In the later stages of a *burned out'* tabes at the height of the organic neurologic findings the laboratory data may be completely misleading The serologic tests of the blood and spinal fluid may be nor mal even when larger quantities are used and the colloidal gold test reads zero in all dilutions The clinician is required to establish the presence of the tabetic involvement by his physical findings despite the denials of the laboratory tests

Course —The course of tabes dorsalis is variable The more obvious and blatant manifestations are those in which there is a progressive ad vance toward invalidism and a fatal issue The comparative rarity of tabes dorsalis in proportion to the number of positive spinal fluid findings in infectious syphilis indicates that most patients pursue a more favor able course An appreciation of these facts is required in the evaluation of therapeutic procedures

Treatment —The treatment of tabes dorsalis is individualized and is dependent upon the stage of the disease and the presenting symptoms

The introduction of *penicillin* in the treatment of symptomatic and asymptomatic tabes holds high promise This prospect contrasts with prior efforts of which Wechsler stated that he had 'never seen a case of tabes cured nor a disappearance of signs once they had become fixed

While it is too soon to assess final results or enunciate an optimum treatment schedule we favor a course of penicillin injections given intra muscularly at three hour intervals for eight to ten days until 10 000 000 units have been delivered We advocate repetition of the course at inter vals of six months until clinical and serologic control is absolute

For the private practitioner we recommend no complicating endeavors We oppose intrathecal therapy with penicillin as with the arsenicals We reserve adjuvant arsenotherapy for those who are penicillin resistant and in whom the risks of treatment are justified Thus far though it is too soon to be dogmatic it appears that penicillin therapy of tabes holds high promise for clinical if not serologic control without *appreciable* added benefits from concomitant arsenotherapy

The patient must be warned of the guarded prognosis and of the necessity for regular reexaminations of blood and spinal fluids He must realize that retreatments at three or six month intervals *are imperative*

TRYPARSAMIDE—The advisability of using *tryparsamide* arises sooner or later in the treatment of each tabetic Those who advocate injections of this drug ordinarily give intravenous injections of 30 to 50 mg per kg (2 2 pounds) of body weight An average adult dose approximates 3 gm dissolved in 10 cc of sterile distilled water Weekly injections are given in courses of 8 to 16 followed by rest periods of approximately six weeks Many clinicians including the present authors have little faith in trypar samide and much fear concerning its toxicity *Untoward manifestations* include tinnitus dizziness nausea vomiting headache urticaria dermati tis jaundice and visual disturbances that may progress to optic atrophy Against these risks there are few positive and convincing evidences of improvement The patient may report gain in weight and a sense of well being but there are no significant changes in the objective findings If the practitioner is driven to its use in desperation he should insist upon pre liminary expert consultation in order to share the onus of toxicologic disturbances

Hyperthermia—The favorable effects of fever treatment in *general paresis* (p 1377) stimulated efforts to apply similar technics for the relief of tabes Unfortunately the same successes have not been experienced and most critical observers including the author reserve hyperthermia for patients whose progress is unsatisfactory despite best efforts with chemo-therapy

Control of Pain—The tabetic in addition to antiluetic therapy re quires palliation particularly relative to the *tabetic crises* For the relief of these agonizing pains many therapeutic endeavors have been instituted and their numbers testify to their relative uselessness Wechsler reports that he has seen no good results from the use of galvanism or faradism albeit they are recommended He states that diathermy may on occa sions give relief to pain and so may x ray therapy (p 3796) This has not been our experience and our only successes are with the daily intra venous injections of large doses of *thiamine chloride* (p 622) Given in amounts of 100 to 200 mg we have had surprisingly satisfactory results when all other measures have failed

Symptomatic *drug therapy* in the tabetic is attended with consider able risk of addiction (p 3815) It is not only the lightning pain but the fear of the onset of these anguishes that lead the tabetic to use increas ingly greater doses of the *analgesics hypnotics sedatives* and *opiates* Many become *chronic alcoholics* in their understandable efforts to secure surcease All else failing localized pain may be subjected to surgical ther apy by *paravertebral injections chordotomy* or *sectioning of the poste rior roots*

Orthopedic Treatment—*Reeducation methods* give excellent results in teaching the tabetic to control his unruly legs *Braces* and *supports* are used to overcome the hyperextensibility of the joints which precedes the tabetic arthropathy

Treatment of Urinary Difficulties—The attention of the therapist often is directed to the problem of dealing with the urinary bladder In the face of urinary retention and dilatation of the bladder it is our belief that optimal management requires the institution of a permanent *supra pubic cystostomy* with fortification by *prophylactic chemotherapy* using

the sulfonamides Repeated catheterization besides being a nuisance in vites urinary sepsis (p 2334)

MENINGOVASCULAR SYPHILIS

In addition to the definitive entities of general paresis (p 1377) and tabes dorsalis (p 1464), syphilis may evoke protean neurologic manifestations due to the production of a meningeal reaction or to involvement of nerve tissue resulting from vascular injury and gumma formation The clinical manifestations are capable of simulating any of the organic diseases of the central nervous system, and the diagnosis is not established until the laboratory findings have been completed In the presence of a positive Wassermann test on blood or spinal fluid of spinal pleocytosis or changes in the colloidal gold reaction the practitioner is entitled to consider, but not definitely to commit himself to the diagnosis of syphilis as the etiologic agent Until the completion of the therapeutic test accomplished by intensive penicillin therapy, hyperthermia (p 3789) and supplementation by iodides for dissolution of the gumma (p 608) there is always the possibility that the syphilitic just as his non infected fellow may be afflicted with an unrelated neurologic disorder such as a brain tumor, meningococcus meningitis or multiple sclerosis for example

PURULENT ENCEPHALOMYELOMENINGITIS

Suppurative inflammations involving brain cord or meninges may be the result of direct extension of pyogenic processes or they may be metastatic in connection with pyemia or amebic dysentery

EXTRADURAL AND SUBDURAL ABSCESS

Subdural and extradural brain abscesses arise as complications of inflammatory processes involving the *skull* the *nasal accessory sinuses* the *middle ear* the *mastoid* or the *lateral superior longitudinal* or *cavernous venous sinuses* (p 1446)

Clinical Manifestations —The complication of brain abscess is usually clouded by the clinical manifestations of the more fundamental process The suspicions of the practitioner are aroused when the systemic manifestations seem out of proportion to the extent of the local process when additional disturbances point to increased intracranial pressure or focal neurological involvements

The signs of *increased intracranial pressure* (p 1421) include headache skull tenderness persistent nausea projectile vomiting congestion of the retinal veins and papilledema *Localizing neurologic signs* are dependent upon the site of the suppuration With *lateral sinus infections* (p 1446) there are irritations of the fifth sixth and eighth cranial nerves as shown by ophthalmoplegia diplopia facial anesthesias or paralysis tinnitus and disturbances in hearing *Frontal lobe abscesses* (p 1469) associated with infections of the orbit and the nasal accessory sinuses are less clearly delineated The patient may reveal subtle changes in disposition delirium or convulsions

Treatment —The approach to the treatment of extradural or subdural abscess involves an attack on the more fundamental lesion Thus in the commonest variety associated with mastoiditis and thrombophlebitis of

the lateral sinus therapy with sulfonamide (p 88) streptomycin (p 103) or penicillin (p 106) is combined with exenteration of the infected bone cells removal of the infected clot ligation of the jugular vein and drainage of the abscessed area in the brain Optimal management requires the cooperation of otologist and neurological surgeon

BRAIN ABSCESS

Brain abscess within the substance of the cerebral hemispheres is most often metastatic It follows *pulmonary suppuration* (p 2219) a generalized *staphylococcemia* (p 153) *amebic dysentery* (p 523) or *pleural empyema* (p 2°22)

Clinical Manifestations—In the majority of instances the intracerebral brain abscess is *asymptomatic* It may persist silently for a period of many years being discovered only by chance at autopsy or as the result of rupture and the secondary production of a *purulent meningitis* (p 1470)

The *symptomatic intracerebral brain abscess* behaves in the manner of *neoplasm* (p 1419) Its presence is suspected when there arise manifestations of *increased intracranial pressure* (p 1468) often with localizing neurological signs Occasionally the spinal fluid reveals increased pressure a pleocytosis with a predominance of lymphocytes or leukocytes

Treatment—Upon suspicion of the presence of an intracerebral brain abscess the *neurosurgeon* is consulted Persistence of the symptoms of increased pressure demand *exploratory craniotomy* Surface abscesses are clearly visible but deeper collections are revealed only by needling

Drainage of the cavity may be followed by remarkable recovery provided that vital neurological structures are not permanently damaged Prophylactic preoperative and postoperative *anti infective therapy* with sulfonamide (p 88) streptomycin (p 103) or penicillin (p 106) greatly reduce the factors of risk

ABSCESS OF THE SPINAL CORD

Abscesses of the spinal cord are rarely observed They may occur as metastatic manifestations of distant purulent processes or in association with staphylococcemia The clinical manifestations are those of cord neoplasm (p 1430) Differentiation is not important since exploratory laminectomy is required in either instance Preoperative and postoperative therapy with penicillin is conducted in the manner of treatment of brain abscess (p 106)

SUPPURATIVE MENINGITIS

Suppurative infections of the meninges may occur by continuity or through the blood stream

Infection by Continuity—Purulent meningitis may complicate compound fractures of the skull as well as orbital nasal and auditory infections Under any circumstance the patient develops manifestations of meningeal irritation including headache stiffness of the neck a positive Kernig sign and opalescent or frankly purulent spinal fluid The most common invading organisms are staphylococci streptococci and pneumococci

Prophylactic anti infective therapy has greatly reduced the incidence of purulent meningitis Moreover this previously fatal complication now

boasts a highly favorable recovery when prompt and intensive therapy is introduced using sulfonamides and/or penicillin (p 106) The latter may be introduced directly into the subarachnoid space by lumbar puncture Despite the efficacy of anti infective therapy adequate surgical drainage cannot be neglected, more particularly in otogenic and rhinogenic in vasions

Hematogenous Purulent Meningitis—Purulent meningitis of hematogen ous origin is usually meningococcal pneumococcal or streptococcal Treat ment is carried out most successfully in the premeningeal phase employing systemic doses of sulfonamide and penicillin (p 106) Following the sec ondary meningeal reaction supplementation is essential in the form of intrathecal instillations of penicillin (p 106)

Suppurative Pachymeningitis—Purulent external pachymeningitis may follow local infection of the meninges by extension from an osteomyelitis of the vertebrae or tuberculous caries Anti infective therapy with sulfo namides and penicillin is warranted under any circumstance for control of secondary invading organisms

CHAPTER 74

THE VOLUNTARY NERVOUS SYSTEM DESCRIPTIVE NEUROLOGY

MANY afflictions of the nervous system are difficult of classification Some are presently recognized as manifestations of *vitamin deficiency* others are obvious *nonbacterial inflammatory processes* the results of *idio pathic degeneration* or *sclerosis* The important conditions of *epilepsy* and *migraine* present no tangible data on which to base nosology

THE PERIPHERAL NEUROPATHIES

Peripheral neuropathies are the commonest neurological disorders They may involve the *cranial* or *vertebral nerves* they may affect one or sev eral nerves

The *mononeuropathies* whether peripheral or cranial include neural gias causalgias and paralytic syndromes They are most often the prod ucts of local pathology but may be of systemic origin *Polyneuropathies* result from exogenous chemicals or drugs but they may follow disturb ances of endogenous metabolism

ANATOMY

The Cranial Nerves.—The cranial nerves are twelve in number The *first* *second* and *eighth* cranial nerves have purely sensory functions and are concerned respectively with smell vision and hearing the *third* *fourth* and *sixth* regulate extra-ocular movements the *eleventh* controls the motor functions of the neck and shoulder and the *twelfth* activates the tongu

The *vagus* or *tenth* cranial nerve is the link with the cholinergic portion of the invol untary nervous system The *adrenergic subdivision* has no corresponding intracranial repre- sentation

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CHAPTER 74

THE VOLUNTARY NERVOUS SYSTEM DESCRIPTIVE NEUROLOGY

- Peripheral Neuropathies
  - Mononeuropathies
    - Cranial
    - Peripheral
  - Polyneuropathies
- Myelopathies
- Encephalopathies
- Scleroses
  - Subacute Combined Sclerosis
  - Amyotrophic Lateral Sclerosis
  - Primary Lateral Sclerosis
  - Progressive Bulbar Palsy
  - Multiple Sclerosis (Disseminated Sclerosis)
- Syringomyelia
- Syringobulbia
- Paralysis Agitans (Parkinson's Disease)
- Migraine
- Histamine Cephalalgia
- Epilepsy

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The *fifth seventh* and *ninth cranial nerves* are mixed in their functions The *trigeminus* is concerned with mastication and facial sensation the *seventh* nerve innervates the facial muscles and shares with the *ninth nerve* the sensations of taste the *glossopharyngeus* has motor functions concerned with the musculature of the pharynx

The Spinal Nerves—The spinal nerves are paired to supply symmetrical portions of the body and extremities They number eight in the *cervical* twelve in the *thoracic* five in the *lumbar* five in the *sacral* and one in the *coccygeal* regions The lower cervical and upper thoracic branches join to form the *brachial plexus* which is concerned with the innervation of the upper extremity the lower lumbar and the upper sacral cord unite in the *lumbosacral plexus* for the legs

Each spinal nerve splits into an *anterior* and *posterior root* as it enters the vertebral column The *anterior root* connects with the *motor horn cell pool* which is situated in the anterior gray matter the *posterior root* connects with the *sensory horn cell pool* in the

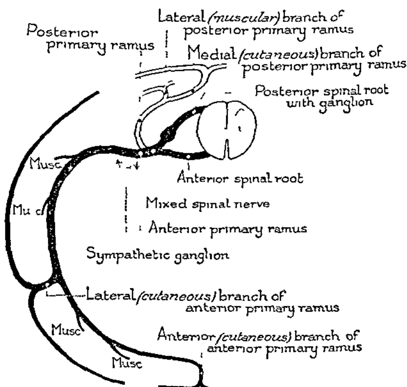


Fig 277—The components of a segmental nerve For purposes of clarity the posterior primary ramus is indicated in outline *Musc* refers to the muscular branches given off by the anterior primary ramus *

posterior gray matter Anterior and posterior horn cell pools are connected in turn each with the other as well as with their fellows of the opposite side and with similar horn cell pools of other segments This arrangement provides for symmetry and coordination of function.

PHYSIOLOGY

The final common pathway is the basic physiological unit of the nervous system *Sensory receptors* are situated in the skin, bones joints and muscles They register touch pain, temperature vibration deep pressure and the sense of position in space Their stimuli are carried through peripheral nerves and into posterior horn cell groups They initiate responses which originate in the anterior horn cell group and pass out through the anterior root and the peripheral nerves to effect adequate responses usually muscular Any lesion of the final

* Haymaker and Woodhall Peripheral Nerve Injuries

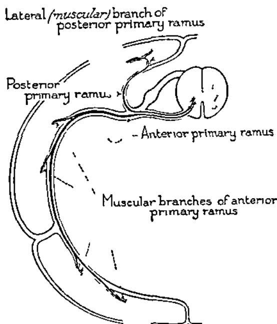


Fig 278—A segmental nerve illustrating the routes traveled by efferent fibers to muscles

Medial (cutaneous) branch of posterior primary ramus
Lateral branch Medial branch
Posterior branch
Lateral (cutaneous) branch of anterior primary ramus
Anterior branch
Anterior (cutaneous) branch of anterior primary ramus
Lateral Medial
Lat sp nothalamic tract

Fig 278A—A segmental nerve showing the course of sensory neurons from the periphery to the spinal cord The fibers indicated by the broken line convey deep sensibility those in solid black touch and those shown as dotted lines pain and thermal sensibility

Haymaker and Woodhall Peripheral Nerve Injuries

common pathway destroys the sensory motor and reflex activities of the individual peripheral nerve and blocks stimuli which might traverse the cord or initiate in the higher centers

The Motor Pathway—The motor activities of the "final common pathway are influenced by *voluntary involuntary* and *postural elements* which are transmitted by separate pathways through the spinal cord Voluntary movement is conducted along the *pyramidal tracts* whose interruption produces spasticity hyperreflexia and abnormal reflexes such as the Babinski Modifications occur through the *extrapyramidal* and the *spinocerebellar elements* Interruptions of the former result in *ataxia* and *abnormal movements* disturbances of the *cerebellar pathway* are marked by *hypotonus* and further *ataxia* as summarized in Table 96

The Sensory Pathways—The important sensory pathways are the *spinothalamic tracts* and *posterior columns* The former is primarily concerned with the recording of *pain* and *temperature* whereas the latter deals essentially with the sensations of *touch vibration* and *position Sensory dissociation* results from the prompt crossing of the spinothalamic tract across the cord whereas the decussation of the fibers of the posterior columns does not occur until the length of the cord has been traversed Thus involvement of *both pathways* may produce a *contralateral* loss of the sensations of pain and temperature but an *ipsilateral* anesthesia ataxia and pallanesthesia as illustrated in Table 96

PAIN

The healthy, normal human being registers few sensory intimations of the existence and the manifold activities of his carcass In the course of the average day, hunger and thirst are experienced the individual becomes fatigued and then rested he is required to urinate and defecate a sexual urge develops which may or may not be gratified Aside from these registrations there are certain sensory messages that bespeak difficulty Of these the most important is pain

THE FUNCTION OF PAIN

Pain is said to be a pleasurable sensation to certain distorted and perverted individuals who enjoy inflicting pain (sadists) or recording pain (masochists) The remainder of the relatively normal human population regards pain as an unpleasurable sensation to say the least Those of a religious turn of mind interpret pain as a punishment or expiation for sin

The practitioner recognizes pain as a fundamentally protective mechanism The child who experiences the pain of a burn keeps away from the fire the adult with abdominal cramps has no interest in food the patient with angina pectoris discontinues activity and rests until the pain has passed In these examples pain has served to prevent further trauma and to secure rest for an anguished part or organ

Pain serves to localize clinical abnormalities Though the sensation may at times be misleading the sufferer reports with subjective accuracy that it is the ear leg or tooth that aches or is sensitive The diagnostician is directed to a more careful investigation of the painful part

Pain may indicate a therapeutic principle The hunger pain of gastroduodenal ulcer emphasizes the principle of frequent feeding Each of us has learned by experience that certain skeletal and muscular discomforts are aggravated by use while others are ameliorated by active motion

Direct Pain—Direct pain is recorded by stimulation of specific nerve endings in skin subcutaneous tissues fascial coverings of muscles and tendons synovia surrounding joints periosteum and parietal lining surfaces of skull and vertebrae and thoracic abdominal cavities

Tegumentary and mucous surfaces are the most richly provided with sensory nerve endings easily demonstrable by pinprick The sensitivity of other structures is best noted in surgical procedures under local analgesia The surgeon may handle muscle tendon cartilage and bone without registration of pain He produces painful stimuli by manipulation of fascial coverings synovia or periosteum Within the body cavities there is sensitivity of parietal membranes but insensitivity of visceral coverings and the viscera themselves The practitioner who performs needling procedures (thoracentesis or abdominal paracentesis) observes that pain occurs when the needle is pushed through skin and again at parietal pleura or peritoneum

The Pathway for Direct Pain—The pathway for direct pain is initiated at punctiform nerve endings throughout the sensitive tissue *Afferent nerve fibers* which transmit sensation from nerve endings gather to form *posterior roots* which terminate in the grey matter of the cord in the region of the posterior column

From the posterior column there is an axone relay which crosses to the opposite side in the grey commissure to enter the lateral funiculi and form the *lateral spinothalamic tract* The painful sensation is carried by the spinothalamic tract to a center in the *medulla* whence it is relayed to the *thalamus* finally registering in the *cerebral cortex*

The Nerve Endings of Painful Sensation—The specific nerve endings which transmit the impulse of pain have a punctiform distribution They vary in their numbers and sensitivities in different regions of the body The finger tips for example are exceedingly attuned to the slightest stimulus

Pain sense is *dissociated* from other peripheral sensations as illustrated in a cocainized area where the practitioner may satisfy himself that the sense of touch is retained though the pain sense has been greatly diminished or even abolished The term *local anesthesia* thus is a misnomer since actually the cocainized area is under *local analgesia*

The Spinal Pathway for Pain—The spinal pathway for pain is so devised that it dissociates pain from touch and produces crossed sensory disturbances

Dissociation of sensation in the cord is best seen in syringomyelia (p 1505) whose lesions involve chiefly the central grey and contiguous portion of the white matter As a result the patient with syringomyelia may present loss of pain and temperature sense in an area which retains the ability to recognize touch Such patients suffer from burns because of inability to recognize that a steam pipe or a hot water bottle which gives a tactile sensation is sufficiently hot to cause a superficial or even a deeper burn

Crossing of the pain sense in the cord is demonstrated in unilateral cervical lesions in which loss of pain sensation occurs on the side opposite to the lesion

The Medullary Pain Center—Nerve endings of the spinothalamic tract probably terminate in a pain center in the medulla The existence of this pain center is clinically suggested by the daily experiences with morphine and its derivatives Without producing local analgesia or unconsciousness the opiate gives blessed relief to all types of pain The site of action

TABLE 96—REACTION PATTERNS OF INJURIES

Level	Muscle Tone	Muscle Strength	Muscle Volume	Abnormal Movements	Superficial Reflex	Deep Reflexes
Primary muscle dystrophy	Diminished	Diminished	Diminished or increased	None	Diminished	Diminished
Peripheral nerve	Diminished	Diminished	Diminished	None	Absent	Absent
Posterior root or horn	Diminished	Diminished	Diminished	None	Absent	Absent
Anterior root or horn	Diminished	Diminished	Diminished	None	Absent	Absent
Pyramidal tract (corticospinal)	Increased	Diminished	Normal	None	Diminished	Increased
Extrapyramidal tract	Increased	Diminished	Normal	Greatly increased See Note 2	Normal	Normal
Cerebellar tract	Diminished	Diminished	Normal	Increased	Normal	Diminished
Spinothalamic atrophy	Normal	Normal	Normal	None	Normal	Diminished
Spinothalamic irritation	Normal	Normal	Normal	None	Normal	Normal
Posterior column atrophy	Normal	Normal	Normal	None	Normal	Normal
Posterior column irritation	Normal	Normal	Normal	None	Normal	Normal

NOTES ON TABLE 96

1 The abnormal reflexes of the pyramidal tract origin include the Babinski and its modifications and clonus

2 The abnormal movements of extrapyramidal origin include tics tremors chorea and athetoses

3 Cerebellar ataxia is equally severe whether the eyes are open or closed

4 Posterior column ataxia is increased by closing the eyes

5 The paresthesias of posterior column irritation include pains such as the lightning pains of tabes and abnormal sensations such as tingling burning itching

Abnormalities of *touch*—Hypesthesia hyperesthesia anesthesia and paresthesia

Abnormalities of *pain*—Hypalgesia hyperalgesia and analgesia

Abnormalities of *temperature*—Thermhyperesthesia and thermanesthesia

Vibration—Pallanesthesia

Dissociation—Loss of the sensations of pain and temperature but maintenance of tactile sensations

is undoubtedly medullary where a center for pain may well be postulated

Thalamic Center—Clinical experience also suggests that there is a pain center in the thalamus Lesions in this area produce the so called thalamic syndrome (Dejerine Roussy) characterized by excruciating

to Peripheral Nerves Cord and Tracts

Abnormal Reflexes	Touch	Pain	Temperature	Vibration	Position	Ataxia	Distribution
Absent	Normal	Normal	Normal	Normal	Normal	None	Irregular
None	Absent	Absent	Absent	Absent	Absent	None	Neuritic
None	Absent	Absent	Absent	Absent	Absent	Present	Segmental
None	Normal	Normal	Normal	Normal	Normal	None	Segmental
Present See Note 1	Normal	Normal	Normal	Normal	Normal	Present	Ipsilateral below medulla
None	Normal	Normal	Normal	Normal	Normal	Present	
None	Normal	Normal	Normal	Normal	Normal	Present See Note 3	Ipsilateral
None	Diminished	Absent	Absent	Normal	Normal	None	Contralateral
None	Diminished	Increased	Increased	Normal	Normal	None	Contralateral
Normal	Diminished	Normal	Normal	Absent	Absent	Present	Ipsilateral
Normal	Paresthesia See Note 5	Normal	Normal	Absent	Absent	See Note 4 None	Ipsilateral

paroxysmal pain in an area that is apparently normal so far as local pathology is concerned Thalamic pain is not allayed by the local use of cocaine nor the medullary action of morphine suggesting a supramedullary center for pain serving as a final relay station before registration in the cerebral cortex

Referred Pain —The surgeon who employs local anesthesia readily demonstrates the absence of direct pain in muscle tendon cartilage bone visceral lining membranes and viscera in cranial thoracic and abdominal cavities Despite the absence of direct pain sensation disturbances of these structures and areas are capable of producing pain by a referred mechanism

Visceromotor and Viscerosensory Reflexes —Referred pain may be produced by spasm of smooth muscle as illustrated by intestinal cramps or labor pains (visceromotor reflex) It may also arise from inflammation of the visceral surface (appendicitis pleuritis meningitis) through the mechanism of a viscerosensory reflex

The viscerosensory reflex registers subjectively and gives objective signs through spasm of striated muscle of the specific dermatome (right rectus spasm in acute appendicitis)

Accurate and Misleading Projection of Referred Pain—The projection of visceral pain may be accurate, as in the localization of the sensation in the right lower quadrant in appendicitis or in the precordium with cardiac difficulties It may on the other hand be bizarre inaccurate and misleading, as for example the pain in the right shoulder with gallbladder disease in the left arm with angina pectoris in the testicles with renal stones and in the knee with disturbances of the hip joint

The Pathway and Mechanism of Visceral Pain—The explanation of the accurate and misleading projection of referred pain rests in an understanding of the pathway and mechanism of referred pain

Each spinal segment supplies a well delineated area of the skin (dermatome) with sensory and motor fibers These same segments also supply autonomic nerve fibers to the various viscera the distribution of which is indicated in Table 97

The stimulus that arises in a diseased organ enters the cord through autonomic fibers and produces an irritability of the cells that also receive direct impulses from the corresponding dermatome Excitation of the spinal cells evokes stimuli that travel in two directions Central stimuli pass to the *thalamus and cerebral cortex there to register as pain* referred to the dermatome whose spinal nerves correspond to the autonomic nerves of the inflamed organ (viscerosensory reflex) Meantime in the local spinal segment the motor efferents are stimulated giving rise to the rigidity of the locally innervated striated muscle Excitation of the sensory afferents produces areas of segmental hyperalgesia (Head zones)

The inflamed viscus through the referred mechanism has produced pain hyperalgesia tenderness and rigidity in the corresponding dermatome which may or may not be in direct anatomical relationship

Referred pain may also arise in an anatomically normal viscus as for example the colic that accompanies disorders of the hollow viscera (stomach intestines urinary passages gallbladder uterus or tubes) The stimulus to pain in an anatomically normal viscus arises when the wall is stretched in the region of a nerve terminal This is best illustrated by considering the physiological disturbances of the stomach When the stomach is empty strong peristaltic contractions arise which give origin to the sensation of hunger These contractions may be greatly increased producing nausea and vomiting but there is no pain so long as there is no distention of the gastric wall Should the pylorus be obstructed the resulting distention of the stomach produces stretching of the wall and referred pain So far as is known the visceromotor reflex manifested by spasm and segmental hyperalgesia (Head zones) are rarely if ever produced by colic alone Their presence strongly suggests anatomical disease (particularly inflammation) Thus spasm of a right rectus indicates a possible appendicitis rather than a bellyache

Recapitulation—1—Knowledge of the mechanism and pathways of direct and referred pain is important to the practitioner in the diagnostic approach and therapeutic management of painful conditions

2—From the diagnostic standpoint the subjective complaint may be caused by direct or distant referred mechanisms Thus left shoulder pain may be due to a subdeltoid bursitis but it may be re-

ferred from a diaphragmatic pleurisy or from a cardiac source Right shoulder pain may be due to a localized myositis or arthritis but it may also be caused by gallbladder colic Pain in the testicle may be due to orchitis but it may also represent renal stone Precordial pain may be derived from a fractured rib or referred from coronary occlusion

3 —Knowledge of the pathway of pain assists in treatment Pain may be allayed locally by heat or cold massage counter irritation immobilization or pressure Local analgesia may be temporarily obtained by cocainization and more lastingly produced by alcohol injection of a nerve ganglion the posterior root or plexus It may be permanently relieved by section of the root

TABLE 97—THE DISTRIBUTION OF AUTONOMIC NERVE FIBERS FROM SPINAL SEGMENTS TO VISCERA*

Viscus	*Spinal Segments*
Lungs	1–7 dorsal mostly [illegible]–5 dorsal
Heart	3–5 cervical 1–8 dorsal predominantly on left side sometimes bilateral
Esophagus	Mainly 5 dorsal also 6 7 and 8 dorsal
Breast	4 and 5 dorsal
Stomach	7 8 and 9 dorsal usually bilateral
Intestine	9–12 dorsal, bilateral or on left side only
Liver	8–10 dorsal on right side
Gallbladder	Mostly 8 and 9 dorsal also 5–7
Kidney	Mostly 10 dorsal, also 11 and 12 dorsal and 1 lumbar
Ureter	11 and 12 dorsal and 1 lumbar
Testis	10 dorsal
Epididymis	11 and 12 dorsal
Bladder	11 and 12 dorsal and 1 lumbar also 3 and 4 sacral
Prostate	10 and 11 dorsal also 1–3 and 5 sacral
Ovary	10 dorsal
Fallopian Tubes	11 and 12 dorsal
Uterine Cervix	11 and 12 dorsal and 1–4 sacral
Uterine Body	10 dorsal to 1 lumbar

After Head from Brain W R Diseases of the Nervous System ed 2 New York Oxford University Press

4 —Relief of pain also may be accomplished centrally by the action of the specific drugs such as the analgesics antipyretics demerol or the narcotics of the opium family Finally in desperate situations it may be necessary to produce general unconsciousness by the use of anesthetics in order to relieve a tortured individual of intractable pain

5 —The therapeutist aims to effect maximum analgesia with minimum side effects He uses first the simpler local measures Not until he is driven to it does he employ drugs that act centrally particularly narcotics which may depress the respiratory center and produce addiction If pain can be strictly localized surgical procedures such as injections with alcohol and posterior root section may be a tremendous boon

6 —In the management of painful conditions the immediate interest of the practical clinician is relief of the local disturbance The general considerations that have been outlined above serve as the

Accurate and Misleading Projection of Referred Pain—The projection of visceral pain may be accurate as in the localization of the sensation in the right lower quadrant in appendicitis or in the precordium with cardiac difficulties It may on the other hand be bizarre, inaccurate and misleading as for example the pain in the right shoulder with gallbladder disease in the left arm with angina pectoris in the testicles with renal stones and in the knee with disturbances of the hip joint

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TRIGEMINAL NEURITIS

Irritative phenomena involving the fifth cranial nerve may result in *trigeminal neuralgia sphenopalatine neuralgia* or *trismus* Loss of function may be followed by *anesthesia* of the skin of the face the anterior half of

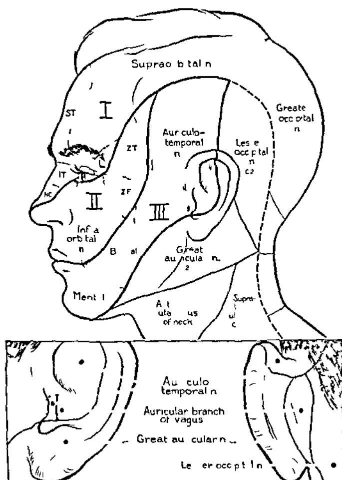


Fig 279 —Diagram of the cutaneous fields of the head and upper part of the neck The three divisions of the trigeminal nerve (I ophthalmic II maxillary III mandibular) are indicated by heavy lines and their respective subdivisions by light broken lines The conjunctivae are innervated by the ophthalmic division Abbreviations refer to the following nerves B buccal IT infratrochlear L lacrymal NC external nasal branch of the nasociliary ST supratrochlear ZF zygomaticofacial ZT zygomaticotemporal The lateral and superior boundaries of the posterior primary rami are indicated by broken lines The inset shows trigeminal and vagal cutaneous fields of the region of the external ear and the external auditory meatus

the scalp the mucous membranes of the lips mouth tongue pharynx accessory nasal cavities teeth and portions of the dura mater the cornea and conjunctiva Abolishment of motor function is associated with *paralysis* of the muscles of mastication and may be central or peripheral

* Haymaker and Woodhall Peripheral Nerve Injuries

enunciation of fundamental principles For purposes of specific information relative to differential diagnosis and treatment of the various conditions management is discussed in this text under the classification of topographic localization (*pain in the head, in the ear in the eye in the abdomen in the chest in the testicles etc*) or physiological function (*dysuria dysphagia dyspepsia etc*)

THE MONONEUROPATHIES

The mononeuropathies are 'reaction patterns that result from pathological involvement of any single nerve whether cranial or peripheral Irritations produce the *neuralgias* or *causalgias* dissolution of continuity causes *atrophy* or *paralysis*

OLFACTORY NEURITIS

Neuritis of the olfactory nerve (I) is most often peripheral in origin Central irritations due to a neoplasm in the region of the uncus or to cerebrovascular disease may produce hallucinations of smell or *parosmia* The latter may also be functional as part of a major *hysteria* (p 1353)

Peripheral involvements result in *hyposmia* or *anosmia* (p 2190) Common examples are impairments or destructions of the nerve endings due to *upper respiratory infection* chronic *nasal sinusitis* with *polyp* formation *atrophic rhinitis vasomotor rhinitis* of allergic origin excessive use of *tobacco* sniffing of *cocaine* and *occupational exposure* to heavy fumes as in the handling of wine Infrequently the olfactory nerve is damaged as the result of a *fracture* through the cribriform fossa meningeal thickening a tumor of the frontal lobe a meningioma or a fibroma involving the nerve or its sheath The majority of peripheral afflictions produce a unilateral loss of sensation which is only manifest when tests are directly made pertinent to this finding

Diagnosis and Treatment—The patient with a unilateral anosmia warrants *specialist consultation* for investigation of a remediable lesion of the nerve itself or of the structures of the anterior fossa in the near vicinity *Neurosurgical consultation* is also warranted when there are hallucinations of smell A bilateral and complete anosmia calls for the opinion of the *rhinologist* since the affliction is almost invariably related to a mucous membrane disturbance

OPTIC NEURITIS

See p 1640

OCULOMOTOR NEURITIS

See p 1645

TROCHLEAR NEURITIS

See p 1647

ABDUCENS NEURITIS

See p 1647

TRIGEMINAL NEURITIS

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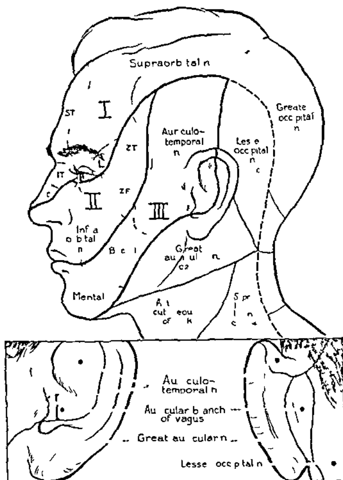


Fig 270—Diagram of the cutaneous fields of the head and upper part of the neck The three divisions of the trigeminal nerve (I ophthalmic II maxillary III mandibular) are indicated by heavy lines and their respective subdivisions by light broken lines The conjunctivae are innervated by the ophthalmic division Abbreviations refer to the following nerve B buccal IT infratrochlear L lacrymal NC external nasal branch of the nasociliary ST supratrochlear ZF zygomaticofacial ZT zygomaticotemporal The lateral and superior boundaries of the posterior primary rami are indicated by broken lines The inset shows trigeminal and vagal cutaneous fields of the region of the external ear and the external auditory meatus

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Haymaker and Woodhall Peripheral Nerve Injuries

TRIGEMINAL NEURALGIA (TRIFACIAL NEURALGIA TIC DOULOUREUX)

Trigeminal neuralgia occurs as a symptomatic or idiopathic complaint In the former instance the disturbance is the result of a neoplasm inflammation or gliosis of the stem, cerebellum or cerebellopontine angle (p 1496) More often the affliction is not associated with demonstrable pathological disease and represents an *irritation of the gasserian ganglion* its roots and its connections with other nuclear cells

Clinical Manifestations—The clinical manifestations of trigeminal neuralgia are characterized by the periodic appearance of transitory attacks of *excruciating pain* involving the sensory areas supplied by one two or three of the branches of the trigeminus In the idiopathic form the condition is seen most often in middle life The pains are of indescribable violence and the sufferer winces and contorts his face in agony Each attack is of short duration but a repetition of the anguish may occur in a few seconds a few minutes or a few hours There may be periods of intermittence of variable length

The attacks of pain are brought on by apparently trivial sensory phenomena such as eating drinking talking exposure to cold washing the face shaving attempts to rest the head on a pillow a loud sound or light touch to trigger zones' which are most often found around the nose and mouth The areas of the *mandibular* and *superior maxillary branches* are affected most commonly but the *ophthalmic division* may also be involved

An idiopathic trigeminal neuralgia is not accompanied by objective neurologic findings Efforts should be made to demonstrate the presence of sensitizing phenomena such as *dental infection* or *inflammation of the nasal accessory sinuses* The presence of *increased intracranial pressure* (p 1491) *tinnitus deafness ataxia* or *areas of anesthesia* requires the practitioner to abandon the diagnosis of an idiopathic neuralgia and refer the patient to the specialist consultant for investigation of an intracranial lesion

Treatment—Idiopathic trigeminal neuralgia despite its tendency to be intermittent does not permanently disappear except as the result of therapy by injection or surgical intervention *Inhalations of trichlorethylene* (p 3864) are occasionally helpful in mild manifestations Palliative measures include *peripheral avulsion* and *injections of alcohol* into the branches of the nerve as they leave the skull The efficacy of avulsion is short lived and the procedure cannot be repeated *Deep injections of alcohol* which may be repeated prove successful in approximately 75 per cent of patients

The radical treatment consists of *injections of alcohol* into the *gasserian ganglion* or of *subtotal to complete section of the sensory root* through a transtemporal or suboccipital approach In expert hands surgical procedures have minimum mortality and maximum promise of success

SPHENOPALATINE NEURALGIA (SLUDER)

Sphenopalatine or vidian nerve neuralgia bears many resemblances to tic douloureux It is differentiated in that it produces a lower half head ache with boring and burning pain in the superior maxillary region and radiation down into the neck and shoulder It may be associated with inflammatory disease of the nasal accessory sinuses and sometimes accom

panies an *ophthalmic migraine* (p 1506) or impaction and infection of maxillary teeth

The *diagnosis* of Sluder s neuralgia is substantiated by the comfort that is afforded by cocainization of the sphenopalatine ganglion Permanent re lief may follow the injection of alcohol and phenol by the experienced expert

SENSORY PARALYSIS OF THE TRIGEMINUS

Sensory paralysis of the trigeminal nerve results in distributional hy pesthesia or anesthesia The site of the lesion may be peripheral or cen tral The former may result from affections of the branches of the nerve as the result of inflammatory processes in the deep tissues of the face or mouth inflammations or neoplasms involving the cranium or the bone that surrounds the various foramina localized meningitis or neoplasms of the pons cerebellum acoustic nerve or the nerve sheaths (von Reckling hausen s disease) Penetrating wounds and fractures of the base of the skull may lacerate the nerve the ophthalmic division is exposed to injury by aneurysms of the internal carotid artery cavernous sinusitis and neo plasms of the hypophysis

Central disturbances dependent upon intra axial involvement include vascular lesions neoplasms of the medulla or pons inflammations such as syringobulbia and epidemic encephalitis and scleroses especially of the disseminated variety

Clinical Manifestations —Sensory paralysis of the trigeminus is char acterized by reduction or loss of the sensations of touch pain and tem perature in the areas supplied by the nerve (p 1481) Trophic changes may result in disturbances of the senses of *smell* and *taste* despite the fact that the former is regulated by the first cranial nerve and the latter by the seventh and ninth In a zoster the characteristic vesicular eruption (p 435) is observed along the path of the involved root Ophthalmic afflic tions whether due to herpes or operative procedures have extreme grav ity since they may be associated with ulcerations of the cornea resulting in permanent opacity and disturbances of vision (p 1626)

Peripheral afflictions are marked by the most complete sensory mani festations dissociation suggests a pathologic process within the neuraxis and sensory disturbances limited to alteration in tactile discrimination point to a more central lesion

Treatment —The management of anesthesia of the trigeminus is di rected towards the elucidation of the cause and its possible elimination Disturbances involving the ophthalmic division call for prophylactic ther apy directed at the cornea (p 1628) Consultation with the ophthalmolo gist is warranted and it may be necessary to suture the upper lids so that the cornea is protected against ulceration

MOTOR TRIGEMINAL IRRITATION

Irritation of the motor branch of the trigeminal nerve results in the production of *trismus* This phenomenon is seen most often in *chilling* when it has little significance On the other hand it is of ominous import as an indication of *tetanus* (p 294) *rabies* (p 439) and *strychnine poisoning* (p 3869)

Tremors of the *muscles of mastication* occur in *paralysis agitans* (p 1505) and *epidemic encephalitis* (p 441)

MOTOR TRIGEMINAL PARALYSIS

Motor paralyses of the muscles of mastication occur peripherally or centrally In the former instance the disturbance is unilateral and may not seriously interfere with the function of chewing Bilateral central paralysis occurs infrequently as a manifestation of *encephalitis* (p 441) or a *supranuclear neoplasm*

PROGRESSIVE FACIAL HEMIATROPHY

Progressive facial hemiatrophy probably results from involvement of the fibers of the involuntary nervous system that accompany the divisions of the trigeminal nerve The condition is apparent from a progressive atrophy of the bone cartilages and soft tissues of the face despite the fact that the muscles show no evidences of degeneration The condition is progressive and may follow injuries to the head and face local infections exposure to cold erysipelas and osteitis of the jaw *Treatment* is of little avail

BELL S PALSY

A peripheral paralysis of the seventh cranial nerve may be *symptomatic* but it is more often *idiopathic* Demonstrable *organic* causes include inflammations and suppurations that involve the nerve at the base of the skull tumors of the acoustic nerve, endotheliomas of the meninges, fractures of the base of the skull and operative procedures involving the mastoid cells In the fallopian canal the nerve may be damaged by otitis media and osteomyelitis of the petrous portion of the temporal bone These major disturbances produce clinical phenomena other than the facial paralysis those which involve the organs of hearing are associated with derangement in the acoustic functions

Much more frequently the Bell s palsy results from some inconsequential circumstance such as the application of ice to the side of the neck or face exposure to draughts or an electric fan or following a hair wash The mechanism of the paralysis is far from clear but it is thought that a perilymphangitis in the unyielding bony canal produces a pressure neuritis

Clinical Manifestations—The idiopathic Bell s palsy comes on rapidly in the course of a few hours It may be preceded by *pain* in the area of the distribution of the nerve but the distinguishing characteristic is *distortion of the face* and *inability to whistle* or *close the eye* The mouth is drawn toward the normal side where its corner is elevated The wrinkles of the forehead and the nasolabial folds flatten The eye appears more widely open on the involved side and the lower lid is often slightly everted so that the mucous membrane is visible Voluntary movements such as the attempts to show the teeth wrinkle the forehead or whistle greatly increase the asymmetrical appearance Saliva drools from the paralyzed side and tearing is noted from the involved eye

In zoster the characteristic vesicles may be apparent on the auricle or within the external auditory canal Idiopathic Bell s palsy is not associated with tinnitus or disturbances in hearing and equilibration

Treatment—The treatment of idiopathic Bells palsy is most unsatisfactory The patient is assured that experience has shown that *spontaneous recovery* is likely to occur The eye is protected with a patch and frequent washings with saline solution The administration of *salicylates* (p 3834) or *iodides* (p 612) is conventionally urged on a purely empiric basis In our experience drugs are of little if any efficacy Local counterirritation can only add to the difficulties but the application of warm wet dressings provides the patient with something to do Doses of *strychnine* (p 3868) are ordinarily prescribed but they accomplish nothing *Electrical treatment* with galvanism or faradism may be suggested in order to keep up muscle tone diathermy (p 3788) is highly regarded by enthusiasts for this form of therapy

SUPRANUCLEAR PARALYSIS OF THE FACIAL NERVES

Supranuclear paralysis of the facial nerve is fortunately uncommon It is differentiated from peripheral involvement as seen in Bells palsy by the failure to involve the superior facial branches which supply the orbicularis and the muscles which produce wrinkling of the forehead

Supranuclear paralysis of the facial nerve is usually associated with an *ipsilateral hemiplegia* (p 1427) and may be due to tumors of the pons hemorrhage into the internal capsule or an encephalitis Associated paralysis of the abducens places the lesion in close proximity to the pons

Symptomatic Bells palsy is treated by an attack on the more fundamental condition Operative anastomoses have been attempted by expert neurosurgeons without consistent success by any of several methods

NEURITIS OF THE INTERMEDIUS (WRISBERG)

The afferent fibers of the intermedius nerve of Wrisberg convey sensations of taste through the glossopharyngeal nuclei efferents join the submaxillary ganglia and transmit secretory impulses to the submaxillary and sublingual glands With inflammations of the *geniculate ganglion* most often seen in *herpes zoster* (p 435) vesicles appear in the external auditory canal and may implicate the motor fibers of the facial nerves Taste is lost over the anterior portion of the tongue Associated involvement of the *auditory nerve* produces tinnitus vertigo diminution in hearing nausea and vomiting

COCHLEAR NEURITIS

Paralysis of the cochlear portion of the auditory nerve (VIII) is almost invariably of peripheral origin The definitive *organic causes* include tumors of the nerve trunk or the cerebellopontine angle (p 1426) a toxic *neuritis* occurs in cinchonism (p 862) and salicylism (p 3834) *inflammations* occur in meningitis scarlet fever typhoid fever tabes dorsalis multiple sclerosis malaria mumps and influenza *Hemorrhages* are encountered in the bleeding diatheses (p 1108) and the nerve termination is often affected in *labyrinthine disease* and *otitis*

Clinical Manifestations—Paralysis of the cochlear portion of the acoustic nerve results in *impairment of hearing* This type of deafness is to be distinguished from that which results from afflictions of the middle ear *Nerve deafness* is characterized by lessened bone conduction but relatively greater air conduction when tested with the tuning fork With the

Rinne test the vibrating tuning fork is heard when held opposite the external auditory meatus after it is no longer recognized when placed upon the mastoid process In the *Weber test* with the vibrating tuning fork placed on the vertex of the skull and occlusion of one and then the other ear the sound is best heard on the normal side (*negative Weber*) In middle or external ear involvement lateralization of sound is on the side of the impaired hearing

Treatment —The treatment of cochlear nerve paralysis involves the elimination of possible etiologic factors such as quinine and the salicylates Otherwise management is directed at the more fundamental disturbance

VESTIBULAR NEURITIS (MENIERE S DISEASE ACUTE LABYRINTHITIS)

Meniere s disease is an acute disturbance of the labyrinth As with other forms of irritative neuritis, the cause is most often *idiopathic* rather than demonstrably organic In the latter instance it may be the result of inflammation of or hemorrhage in the labyrinth as the result of the various infectious diseases especially syphilis and the hemorrhagic phenomena More often Meniere s disease like trigeminal neuralgia occurs recurrently and without obvious pathological manifestations

Clinical Manifestations.—The acute attack of Meniere s disease is characterized by the sudden onset of intense dizziness vomiting disturbances in equilibrium and nystagmus Except for the labyrinthine phenomena the examination reveals no significant abnormality and the attack passes only to recur after a variable interval In our experience many of the patients with Meniere s disease suffer psychogenic disturbances

Treatment —The patient with Meniere s disease may be assured that recovery will be noted within a few hours to a few days with or without treatment Bed rest is required in a quiet and darkened room sedatives and hypnotics are administered in generous doses

Intranasal Treatment—If there is a history of a recent respiratory infection or the patient is known to have chronic inflammation in the nasal or auditory passages specialist consultation is advisable A blockage of the *eustachian tube* may be alleviated by use of vasoconstrictor substances introduced intranasally (p 2027) or actual catheterization of the passageway by an experienced expert

Dietotherapy —Those who incline to the theory of the metabolic origin of Meniere's disease have demonstrated a *retention of sodium* in the body Following this clue they suggest the use of a restricted sodium diet of low salt content This list of foods to be avoided or taken sparingly includes salt meat and fish salted bread and crackers and salt butter Carrots clams condensed milk raisins caviar peas olives spinach cheese endive oysters lima beans beets buttermilk cantaloupe cauliflower celery chard dried cocoanut dried currants dates figs horseradish kohlrabi limes musk melons peanuts peach mustard pumpkin radishes rutabagas strawberries turnips turnip tops and escarole are on the restricted list All foods are prepared and served without salt

The dietary routine is supplemented by the administration of 3 gm *ammonium chloride* taken three times daily for three days with a two day holiday

Potassium Therapy —The success of the low sodium routine suggested

that the favorable outcome was attributable to a relative *hyperpotassemia* As a substitute for the cumbersome diet 1 gm potassium chloride has been administered at two hour intervals without dietary restrictions A teaspoonful of *25 per cent potassium chloride solution* represents an approximate dose and a trial for three weeks is recommended

Surgery—Meniere s disease can be relieved by partial root section of the involved auditory route The procedure is performed through a cerebellar approach and is reserved for incapacitating examples which fail to respond to low sodium or high potassium therapy

Miscellany—As in the case of all self limited diseases many cures for Meniere s disease are reported They include injections of histamine thiamine chloride niacin strychnine and neurophosphates

SEASICKNESS

The syndrome of seasickness is included with the present material since there is a suggestion that the disturbance results from overstimulation of the equilibratory mechanism of the internal ear The clinical manifestations are all too familiar and consist of epigastric discomfort anorexia salivation headache dizziness weakness a greenish pallor dejection and bouts of nausea and vomiting

Treatment—Despite the many adherents to the *psychogenic theory* of the origin of seasickness we incline to the belief that the disturbance is functional in a labyrinthine sense

Prevention—Prophylaxis by the generous use of *sedatives* and *hypnotics* prior to the voyage is helpful More recently repeated doses of *amphetamine sulfate* (benzedrine) have won adherents though the resultant sleeplessness and restlessness add to the awareness of discomfort Many experienced travelers favor inhalations of 100 per cent oxygen or the use of hyoscine (gr 1/100) with or without *barbiturates* or *chlorbutanol*

A time honored prescription consists of *chloral* and *sodium bromide* as undernoted

℞		
℞	Sodium Bromide	15 0
	Chloral Hydrate	8 0
	Syrup of Oran e Peel q.s a d	60 0

Sig 1 teaspoonful every 3 hrs for 4 doses preceding the voya e

Seasickness may be mitigated by a *fast* of at least twelve hours and a *purge* taken at the beginning of the fast On boarding ship the susceptible patient is ordered to *recline in bed* for at least the first twenty four hours of the trip The doses of the *bromide and chloral mixture* are continued food intake is limited to tea and toast ingested in a *semirecumbent position* If the diet of tea and toast becomes monotonous carbonated drinks such as dry ginger ale or champagne act as carminatives and combat dehydration The room is freely *ventilated* and *darkened* The *ears* are plugged with cotton and a tight *abdominal binder* is applied particularly in the visceroptotic (p 3488)

Active Treatment—With the onset of seasickness the prophylactic measures are supplemented by intravenous injections of 50 cc of 50 per cent *dextrose* and subcutaneous hypodermics of 1/80 grain of *atropine sulfate* or 1/100 grain of *scopolamine hydrobromide* (*hyoscine*) The addition

of *strychnine sulfate* despite its advocates seems irrational *Amphetamine sulfate (benzedrine)* is used in larger dosages, such as 10 to 20 mg with reported spectacular improvement in 80 per cent of those treated Inhalations of 100 per cent *oxygen* are recommended and other favored measures include the generous use of *chlorbutanol* (chloretone) in doses of 6 to 9 grains Injections of morphine seem to be hazardous because of the frequent tendency of morphine to produce vomiting as an untoward effect

GLOSSOPHARYNGEAL NEURALGIA

The *petrosal and jugular ganglia* of the ninth nerve may be affected in the manner of a trigeminal neuralgia (p 1482) The disturbance is most often idiopathic and rarely, if ever, associated with organic findings

Clinical Manifestations —Glossopharyngeal neuralgia is characterized by spasms of excruciating lancinating *pain* which radiates from the *pharynx* and the *tonsillar fossae* to the *ear* The pain may be initiated by swallowing or yawning it lasts from a few seconds to a few moments and may recur many times Usually the attacks are intermittent and separated by long free intervals

Treatment —The treatment of glossopharyngeal neuralgia is less satisfactory than that of the trigeminal variety Paroxysms may be lessened by *cocainization* of the pharynx and tonsillar areas but alcohol injections cannot be accomplished In severe examples the expert neurosurgeon attempts *peripheral avulsion* which affords temporary relief *Intracranial division of the nerve* proximal to the ganglia, is necessary for a permanent amelioration of symptoms

GLOSSOPHARYNGEAL PARALYSIS

Isolated paralysis of the ninth nerve is not observed since the structure is never damaged without coincidental involvement of spinal accessory and vagus The symptoms and signs of glossopharyngeal involvement include *anesthesia* of the upper portion of the pharynx *loss of the sense of taste* over the posterior third of the tongue *difficulty in swallowing* and *abolition of the pharyngeal reflex*

VAGAL NEURITIS

The condition of *vagotonia* is discussed with the disturbances of the involuntary nervous system (p 1395)

VAGAL PARALYSIS

Vagal paralysis is an exceedingly *ominous circumstance* that is associated with inflammations scleroses tumors and vascular accidents involving the medulla Toxins such as alcohol lead and arsenic are said to influence this vital structure whose interruption results in unilateral paralysis of palate pharynx and larynx The voice assumes a nasal quality and difficulty is noted in swallowing Palatal and pharyngeal reflexes are absent and the corresponding vocal cord assumes the cadaveric position (p 2091) Disturbances occur in cardiac and respiratory rates and rhythms

PARALYSIS OF RECURRENT LARYNGEAL NERVE

Paralysis of the recurrent laryngeal nerve constitutes the most frequent injury to any division of the vagus This branch is quite vulnerable

and its function may be arrested following accidental severance during *operations on the thyroid* in *aneurysms of the aorta* in *enlargements of the left auricle* as in a tight mitrostenosis and in *inflammatory and neo plastic processes of the mediastinum*

The condition is suspected when the patient complains of **hoarseness** and the quality of the voice exhibits little change Examination of the larynx reveals the affected cord in a position midway between abduction and adduction (p 2091) There is no movement on phonation or respira tion

Complete *bilateral recurrent laryngeal paralysis* produces total aphonia a lack of closure of the glottis in coughing difficulty in breathing respira tory stridor and dyspnea

PARALYSIS OF THE SUPERIOR LARYNGEAL NERVES

Isolated paralysis of the superior laryngeal nerves is infrequent it is associated with hoarseness a lowering of the pitch of the voice and a tend ency of food to enter the larynx

Treatment —The treatment of paralyses of the laryngeal nerves calls for specialist consultation with the laryngologist (p 2025) Spasm of the glottis may require measures to prevent asphyxiation

NEURITIS OF THE SPINAL ACCESSORY NERVE

Paralysis of the eleventh cranial nerve may result from disturbances of the upper cervical region or the nerve trunk in the neck In the former instance the lesion may be a *poliomyelitis* a *progressive muscle atrophy* a *gliosis* or a *tumor* *Peripheral paralysis* results from caries of the upper cervical vertebrae neoplasms localized meningitis or injuries during opera tions on the cervical glands in the resection of a cervical rib or in asso ciation with a fracture of the base of the skull

Clinical Manifestations —Paralysis of the eleventh nerve produces motor disability of the *sternomastoid* and the *trapezius* As a result the patient is unable to turn the head toward the opposite side the shoulder droops and cannot be elevated the scapula is displaced downward and outward with external rotation

NEURITIS OF THE HYPOGLOSSAL NERVE

Central involvement of the twelfth nerve is a common accompaniment of the lesions that produce *hemiplegia* particularly the *vascular accidents* (p 1439) The nucleus becomes involved in *bulbar palsy* (p 1504) *syrin gobulbia* (p 1505) *tabes dorsalis* and diseases of the *medulla oblongata*

The *nerve trunk* may be injured in the posterior cranial fossa by tumors meningeal inflammations hemorrhages aneurysm of the vertebral artery fractures of the skull and inflammations of the bone

Clinical Manifestations —Hypoglossal paralysis is manifested by *devia tion of the tongue* toward the paralyzed side This results from the un opposed action of the opposite genioglossus Speech is little affected by unilateral paralysis

PERIPHERAL MONONEUROPATHIES

The mononeuropathies that involve the peripheral nerves most often result from *local trauma* Irritations produce neuralgias or causalgias

TABLE 98 —PERIPHERAL NERVE INJURIES

Nerve Involvement	Common Etiologies	Motor Signs	Sensory Signs
Cervico occipital neuralgia	Focal infection Spheno ethmoiditis		Pain spasm and stiffness in regions of C 1–4
Phrenic nerve	The polyneuropathies (p 1499) Lead poisoning (p 762) Alcoholism (p 3848) Diphtheria (p 302) Aneurysm of carotid Neoplasms or injuries in neck (p 3509) Aneurysm of aorta (p 98) Mediastinal neoplasms Poliomyelitis (p 457) Neoplasms of cord (p 1430)	Dry nonproductive cough Intractable hiccough (p 1933) Ipsilateral paralysis of diaphragm	
Long thoracic nerve	Supraclavicular wounds and strains	Scapulae winged	
Suprascapular nerve	Blow on shoulder	Subluxation of humerus	
Axillary nerve (circumflex)	The polyneuropathies (p 1499) Fractures of the surgical neck of the humerus (p 3018)	Paralysis of deltoid *Inability to abduct the arms*	
Musculocutaneous	Fracture or dislocation of humerus	Paralysis of flexion of forearm Biceps reflex lost	Anesthesia of outer anterior surface of forearm
Radial nerve (musculospiral)	Compression during sleep Compression during operation Compression from splint during intravenous drip The polyneuropathies (p 1499) Plumbism (p 762) Trauma to forearm	Paralysis of extensor muscles of elbow Paralysis of triceps Wrist drop Finger drop	

Median nerve	Trauma to arm, forearm or wrist	Weakness or absence of pronation of forearm Weakness or absence of radial flexion of the wrist Hand deviates to ulnar side Weakness or absence of flexion of metacarpophalangeal and phalangeal joints of the index and middle fingers Weakness or absence of flexion of the terminal phalanges of thumb Weakness or paralysis of abduction and opposition of thumb to fingers	Causalgia along sensory distribution with incomplete involvement
Ulnar nerve	The polyneuropathies (p 1409) Injury at the elbow or wrist	Paralysis of ulnar flexors of wrist Deviation of the wrist to radial side Paralysis of the flexors of the interphalangeal joints of the ring and little fingers Paralysis of the muscles of the hypothenar eminence Inability to abduct and flex the little finger Paralysis of the interossei and lumbricales Inability to adduct and abduct the fingers Inability to flex the metacarpophalangeal joint of the fingers Weakness of abduction of thumb	
Anterior crural (*femoral*) nerve	Diabetes mellitus (p 1240)	Thigh cannot be flexed on trunk, leg cannot be extended Knee jerk lost	Anesthesia of inner side of thigh and leg
Intercostal neuralgia	Herpes zoster (p 435)		Girdle pain

TABLE 98 — PERIPHERAL NERVE INJURIES (*Continued*)

Nerve Involvement	Common Etiologies	Motor Signs	Sensory Signs
Lateral femoral cutaneous nerve	Tight corseting Fascial pressure *Pes planus* Obesity Cord tumor		Meralgia paraesthetica (pain in antero-external part of thigh) Anesthesia of region
Sciatic (extraspinal involvement) nerve	Local infection Local neoplasm Pressure from pelvic neoplasm Pressure from pelvic inflammation		Sciatica
Sciatic (extraspinal) nerve	Osteoarthrosis of hip *Dislocation of hip* Fracture of hip or thigh *Gluteal injection* Brodie's abscess (p 2982)		
Sciatic (intraspinal involvement) nerve	Herniation of the *intervertebral disk* (p 3074) Tuberculosis syphilis osteomyelitis or metastases in lumbar *and sacral vertebrae* Osteoarthrotic spurs of lumbosacral spine (p 2855) Back strain (pp 3063 3071) The polyneuropathies (p 1499) Arteriosclerosis of nutrient vessels	Paralysis of flexors of the knee Paralysis *of muscles* below the knee Inability to lift leg from the floor Foot drag	Sciatica

Common peroneal nerve (the external popliteal)	The polyneuropathies (p 1499) Injury to upper end of fibula Compression at upper end of fibula during sleep by bandages or through occupation Plumbism Arteriosclerosis of nutrient vessels	Atrophy and paralysis of anterior leg muscles Foot drop Loss of eversion and inversion of foot	
Tibial nerve (internal popliteal)	The polyneuropathies (p 1499)	Atrophy and paralysis of muscles of the calf and plantar muscles of foot Weakness or paralysis of extensors of ankle Weakness or paralysis of flexors of the foot Weakness or paralysis of the flexors of the toes Atrophic ulcer of heel	
Coccydynia	Trauma Conversion hysteria		Pain in coccyx
Metatarsalgia	Bad foot mechanics		Pain in 4th metatarsophalangeal articulation
Plantar neuralgia	Footstrain		Numbness and hyperesthesia in tips of toes and ball of great toe

Fig 280—The cutaneous fields of peripheral nerves from the posterior aspect. The boundaries of cutaneous supply of the posterior primary rami are indicated by broken lines. The designation *Post cut rami of thor ns* refers to the cutaneous branches of the posterior primary rami. *Lat cut rami* indicates the distribution from the lateral branches of the anterior primary rami. For purposes of orientation the spinous processes of the first thoracic (T1), the first lumbar (L1) and the first sacral (S1) vertebrae are indicated by arrows.

* Haymaker and Woodhall, Peripheral Nerve Injuries

best illustrated by the *sciaticas* (p 3072) more complete injuries result in *paralyses* of motor nerves and *anesthesias* in the region of sensory structures

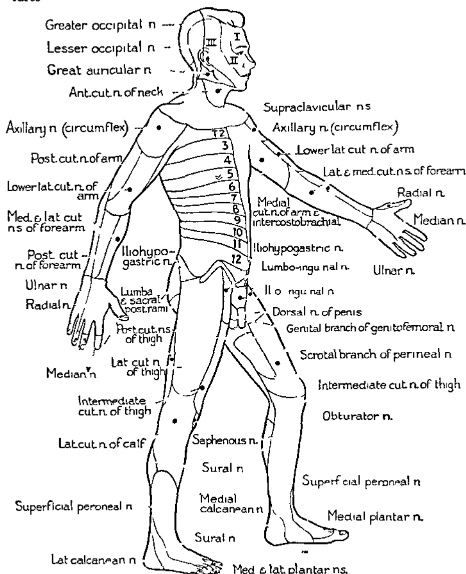


Fig 281.—Side view of the cutaneous fields of peripheral nerves The face and anterior half of the head are innervated by the three divisions of the trigeminal I ophthalm II maxillary III mandibular The fields of the intercostal nerves are indicated by nume l The unlabeled cutaneous field between great and second toe is supplied by the deep peroneal nerve

Mononeuropathies also arise as the result of an *elective localization* of a generalized systemic process Isolated musculospiral involvement producing wristdrop and footdrop from an affliction of the external popliteal

Haymaker and Woodhall, Peripheral Nerve Injuries

nerve may result from arsenical poisoning despite the absence of other demonstrable changes in the nervous system

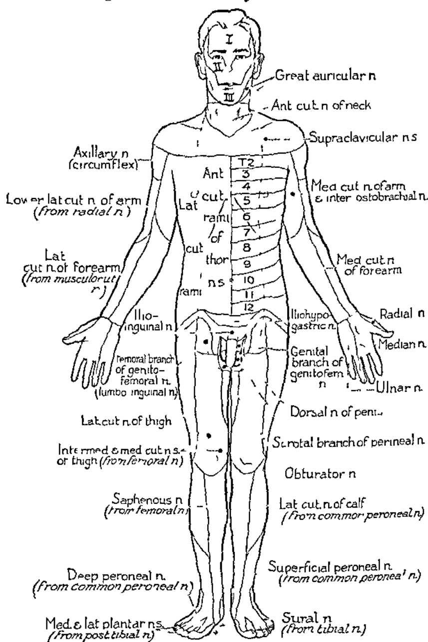


Fig 282—The cutaneous fields of peripheral nerves from the anterior aspect The numbers on the left side of the trunk refer to the intercostal nerves On the right side are shown the cutaneous fields of the lateral and medial branches of the anterior primary rami The asterisk just beneath the scrotum is in the field of the posterior cutaneous nerve of the thigh *

Clinical Manifestations—The clinical manifestations of the peripheral mononeuropathies are listed in Table 98 together with the common etiologies and the motor and sensory signs (p 1490)

Haymaker and Woodhall Peripheral Nerve Injuries

Diagnosis—The diagnostic investigation of a peripheral mononeuropathy differs in each instance In general the local causes include trauma congenital anomalies and the presence of local inflammatory processes or neoplasms The trauma may be *acute* as in the instance of a fracture or it may be *chronic* as in metatarsalgia The injury may be of recent origin or it may be long standing

The *local inflammatory processes* that cause impingement on a nerve are most often exudative articular processes particularly the *osteo-arthroses* (p 2855) In these the spurs press upon the trunks as they emerge from the vertebral column Less often the disturbance is caused by a *neoplasm*

Extraordinarily elective localizations are occasionally observed when a single nerve becomes affected in a systemic disturbance In the absence of definitive proof of local impingement the practitioner seeks more distant

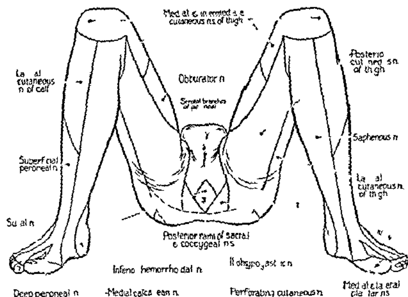


Fig 233—Perineal view of the cutaneous fields of peripheral nerves

etiologic factors These include *focal infections* (p 42) or the occurrence of *neurotropic infections* such as herpes zoster and poliomyelitis *poisonings from chemicals* used in cosmetics or occupationally or by *drugs* administered for purposes of therapy *intoxications* resulting from metabolic diseases as in the instance of diabetes mellitus or an *avitaminosis*

Treatment—The treatment of mononeuropathy depends upon its causative agency *Local causes* are often corrected by appropriate surgery including adequate reduction of a fracture removal of exuberant callus division of an anomalous scalenus anticus or excision of the herniated nucleus pulposus *Offending drugs and chemicals* are eliminated and *endogenous intoxications* are ameliorated by controlling a disturbance such as a diabetes mellitus *Foci of infection* can be attacked by the dentist or the rhinologist

Haymaker and Woodhall Peripheral Nerve Injuries

TABLE 99 —DISTURBANCES OF THE PLEXUSES

Nerve Involvement	Common Etiologies	Motor Signs	Sensory Signs
Brachial plexus (upper radicular involvement)	Trauma to the supraclavicular space Fracture of clavicle Neoplasms of supraclavicular space Birth trauma (p 2951) See *Erb paralyses* *Klumpke paralyses*	Arm hangs limply at side Absence of abduction of arm Absence of lateral rotation of arm Absence of outward rotation of arm Absence of flexion of elbow Absence of biceps reflex	
Brachial plexus (lower radicular *involvement*)	Cervical rib *Scalenus anticus syndrome* (p 2953) Trauma to humerus *Forceful reduction of fractures of humerus*	Feeble radial pulse *Vasomotor changes and trophic changes in* skin of affected arm *Horner's syndrome* (p 1400)	Pain in shoulder and arm
Lumbosacral plexus	See *sciatic nerve* (p 1492)	See sciatic nerve and additionally Weakness and sensory involvement of anterior thigh and buttocks	
Cauda equina	See *cord tumors* (p 1430)		

Palliation—Palliative treatment of a mononeuropathy is often highly effective *Analgesics* are administered orally as acetylsalicylic acid or the salicylates Severe pains require additionally the use of an *opiate* preferably codeine Considerable comfort is afforded by the application of *heat* using an electric pad a hot water bottle hot compresses an infra red lamp or *diathermy* Enthusiasts for the last form of therapy claim specificity of results but our own experiences leave us in doubt whether this modality accomplishes more than any other form of heat (p 3783) We have no great confidence in *electrotherapy* whether by galvanism or *faradism* *Paralyzed muscles are best prevented from stretching* by the application of splints as in foot and wrist drop *Massage* can do no harm and is certainly of psychotherapeutic efficacy (p 3766)

Counterirritation is employed almost invariably with or without the consent of the physician *Oil of Wintergreen* (p 3122) is the most popular of the ingredients and its use has the recommendation of custom Intravenous injections of 100 to 200 mg of *thiamine chloride* are *worthy of trial* through the experience of their extraordinary efficacy in the management of tabetic crises (p 1467) Local *freezing* with ethyl chloride is sometimes helpful in herpes zoster

Surgery—Intractable pain requires more vigorous therapy Temporary relief is often afforded by injection or infiltration of trigger points with *procaine* for temporary effect and *alcohol* for more permanent relief Excruciating and intractable anguish may require the *intraspinal division* of the *sensory root*

POLYNEUROPATHIES

Polyneuropathy refers to the great group of peripheral nerve involvements with multiple manifestations As opposed to the mononeuropathies they are never due to local pathology but always result from systemic cause

Etiology—Despite the many different precipitating causes for polyneuropathy each agency eventually damages the nerve tissue by producing vitamin deficiency local ischemia or chemical destruction

See *Beriberi* (p 625) *Pellagra* (p 625)

The more common etiologic agents or precipitating factors include alcohol lead arsenic triorthocresyl phosphate mercury phosphorus carbon monoxide carbon disulfide benzene sulfur thallium acetate and sulfonamides Many of the disturbances attributed to injections of serums infectious diseases blood dyscrasias metabolic disturbances and systemic disease of unknown etiology are probably specific vitamin deficiencies due to inadequate food intake inadequate gastro intestinal absorption or inadequate assimilation of food

Clinical Manifestations—Involvement of the nerves begins most frequently in the lower extremities with *pains* in the muscles of the calves and feet The discomfort may be sharp lancinating dull or boring with associated tenderness pins and needles *sensations or burning of the* soles toes and feet Coincident with preceding or following the *paresthenas weakness* of the feet and ankles is noted when small objects cause tripping and there is difficulty *in walking in the dark*

The pains may persist or be replaced by *numbness* The pain ascends higher in the limb while the burning of the soles of the feet continues

TABLE 99.—DISTURBANCES OF THE PLEXUSES

Nerve Involvement	Common Etiologies	Motor Signs	Sensory Signs
Brachial plexus (upper radicular involvement)	Trauma to the supraclavicular space Fracture of clavicle Neoplasms of supraclavicular space Birth trauma (p 2951) See *Erb paralyses* *Klumpke paralyses*	Arm hangs limply at side Absence of abduction of arm Absence of lateral rotation of arm Absence of outward rotation of arm Absence of flexion of elbow Absence of biceps reflex	
Brachial plexus (lower radicular involvement)	Cervical rib Scalenus anticus syndrome (p 2953) Trauma to humerus Forceful reduction of fractures of humerus	Feeble radial pulse Vasomotor changes and trophic changes in skin of affected arm Horner's syndrome (p 1400)	Pain in shoulder and arm
Lumbosacral plexus	See *sciatic nerve* (p 1492)	See sciatic nerve and additionally Weakness and sensory involvement of anterior thigh and buttocks	
Cauda equina	See *cord tumors* (p 1430)		

MYELOPATHIES

Toxic involvement of the spinal cord may be the result of the operation of those factors responsible for the peripheral neuropathies (p 1489) Manifestations are most commonly seen as the result of deficiency of niacin (p 620) as in *pellagra* (p 625) in *primary hyperchromic macrocytic anemia* (p 1077) with *poisonings* by carbon monoxide carbon sulfide and chloroform The traumatic myelopathies follow spinal and particularly caudal and epicaudal injections for anesthetic purposes

The clinical manifestations of any toxic myelopathy may be those of a degeneration of the *posterolateral columns* as in *tabes* (p 1464) there may be essential *pyramidal tract involvement* producing a spastic condition The presence of syphilis of the cord or a blood dyscrasia is eliminated by examinations of the hemogram the blood and spinal fluid serologies

Treatment requires the elimination of toxic agencies the administration of a high vitamin diet with accessory parenteral injections of all available preparations and the prevention of urinary sepsis

Caisson Disease —An almost specific involvement of the spinal cord seems to occur in caisson disease (diver s paralysis) Persons subjected to high atmospheric pressure as in diving or working under compressed air in a caisson develop these manifestations when they are suddenly returned to lowered or normal pressures On surfacing the rapidly decompressed worker complains of headache dizziness head pressure pains in the pit of the stomach (*the bends*) and pains in the limbs and back A complete or partial paralysis may develop involving both lower extremities The paraplegia is accompanied by varying degrees of sensory loss below the level of the lesion and there may be retention or incontinence of urine as in a transverse myelitis (p 1457)

Treatment requires prophylactic measures in that decompression is accomplished slowly and gradually

ENCEPHALOPATHIES

The encephalopathies are similar in their etiology to the polyneuropathies (p 1499) Most often they are due to *avitaminosis* or to chemical or pharmacological causation Common examples are seen in *alcoholism beriberi pellagra* and poisonings with *arsenic lead* or *mercury*

Clinical Manifestations —The clinical manifestations of a toxic encephalopathy are best illustrated in the experiences with *arsenotherapy* in syphilis (p 124) As a manifestation of sensitization rather than over dosage the patient becomes *irritable drowsy* and *confused* The symptoms may be mild and transitory or they may progress to *profound coma* or violent agitation with *convulsions* The *spinal fluid* is under increased tension but shows no other abnormality Autopsy fails to reveal the hemorrhagic manifestations that are said to exist in this condition and shows little change other than edema and round cell infiltration of the vessels

Treatment —The encephalopathy is best treated by *repeated lumbar drainage* and injections of 50 to 200 cc of 50 per cent *sucrose* Antidotal drug therapy is more apt to produce additional difficulty than amelioration of symptoms Injections of *sodium thiosulfate* and *cevitamic acid* have been of no value in our experience

The feet seem cold to the touch and are no longer dependable in recording the temperature of the bath The disability in walking is increased by involvement of the primary sensory modalities of *vibration* and *position sense* The same set of symptoms may appear in the hands and progress with the leg involvement As a rule there is no involvement of cranial nerves bladder or bowel

Neurologic examination reveals *flaccid atrophy* most marked in the feet and legs *impairment of the primary sensory modalities* greatest in the most terminal portions of the extremities, *hyperpathia* before there is complete loss of sensation and *trophic disturbances* most marked when the muscle and sensation are most involved

Certain of the specific neuropathies have characteristic clinical phenomena Those due to *alcohol* (p 1385) are often associated with bilateral footdrop and a resultant steppage gait resembling a *tabes* (p 1464) The *lead neuropathies* are often predominantly motor and associated with colic and encephalopathy (p 762) The palsy is often more prominent in the upper extremity and may be unilateral particularly causing wristdrop In *diphtheritic palsies* (p 302), the cranial nerve involvement is often predominant *Arsenical polyneuropathies* are prone to involve all four extremities and practically all muscle groups There may be an accompanying optic atrophy and encephalopathy ordinarily referred to as *hemorrhagic encephalitis* (p 124)

The polyneuritis of *thiamine chloride deficiency* (p 623), described as the clinical entity of *beriberi* is usually associated with a persistent edema and circulatory manifestations due to involvement of heart muscle The *pellagrous type of vitamin B deficiency* in addition to the peripheral neuropathy exhibits more marked evidences of degeneration of the posterior and lateral columns of the cord as seen in a combined degeneration (p 1502) The syndrome of *acrodynia* (erythredema polyneuritis) is probably a representation of vitamin deficiency as it occurs in infants and young children

Diagnosis—Polyneuropathy is such a clearcut reaction pattern that it can rarely be confused A search is required for the factor or factors which produce the etiological disturbances and their secondary reverberations in the central and peripheral nervous system

Treatment—The prime aim of therapy requires elimination of toxic factors and the immediate correction of the dietary deficiency by *adequate diet* and the use of *accessory vitamins* All of the vitamins are given since most of them are capable of producing changes in the central nervous system The vitamin intake of an adequate diet is often quite sufficient but if there is disturbance in gastro intestinal absorption the vitamins are given by parenteral injection using *thiamine chloride riboflavin* and *niacin* (p 620)

Physiotherapy is used for patients with wrist and footdrop Adequate splinting of the wrist is applied in the mid position and the use of splints or pillows at the bottom of the bed prevents stretching of the peroneal muscles *Massage* is given to maintain the tone of the muscle providing it does not induce pain If there is pain or tenderness of the muscles moist heat in the manner prescribed by Sister Kenny is used until pain and tenderness have disappeared

THE SCLEROSES

The scleroses constitute a baffling and discouraging group of neurological disorders Their etiologies are unknown and treatment is of no avail

Subacute Combined Sclerosis

Subacute combined sclerosis is a *degenerative disease* of the spinal cord which usually begins after middle age It involves the *posterior horns posterior columns* and the *pyramidal tracts* The pathological manifestations were formerly seen much more frequently in the era that preceded liver therapy of *macrocytic hyperchromic anemia* (p 1077) There is a strong likelihood that present syndromes result also from metabolic causes

Clinical Manifestations —The symptoms and signs of subacute combined sclerosis are variable *They may resemble a tabetic syndrome* (p 1464) or appear as a *spastic monoplegia* or *paraplegia* *Painful paresthesias* are noted referable to the extremities The spinal fluid examinations are normal excluding *tabes dorsalis* blood counts and bone *marrow studies reveal* none of the phenomena of *hyperchromic macrocytic anemia* there is no satisfactory *therapeutic response* to the administrations of *liver and liver extracts* (p 1081)

Treatment —Treatment involves the elimination of any general hygienic error Therapeutic trials with *crude liver extract* or *bismuth* and *iodides* are warranted The suspicion of a cord tumor with or without positive spinal fluid findings (p 1434) warrants *exploratory laminectomy*

Amyotrophic Lateral Sclerosis

Amyotrophic lateral *sclerosis erroneously called chronic poliomyelitis* is a relatively rare disease It begins at the age of thirty five to forty and is more frequent in foreign born than in native Americans It is chronic and progressive and terminates fatally *in four to five years* The pathologic changes are confined to the *anterior horn cell groups* and the *pyramidal pathways* Degeneration of the gray matter in the motor strip of the brain cortex has also been found at autopsy

Clinical Manifestations —Amyotrophic lateral sclerosis usually is initiated by *symmetrical atrophy of the hands feet or tongue stiffness* and *weakness* Atrophy *of the tongue is associated with difficulty of swallowing* and chewing The involvement of muscles follows a bilateral symmetrical segmental distribution and the atrophy is associated with *spasticity hyperreflexia* and the appearance of pathological phenomena such as *clonus* and the *Babinski signs*

Course and Treatment —The course of the disease is that of progression until the *cranial nerve* nuclei are involved with eventual fatal termination It was thought that the administration of *vitamin E* (p 629) might arrest the progress of the disease but more objective studies have failed to show any *specific therapeutic benefits*

Primary Lateral Sclerosis

Primary lateral *sclerosis is an uncommon* disturbance of unknown etiology in which there is a *pure pyramidal tract degeneration* As a result the condition is characterized by gradually increasing *motor weak*

ACUTE SUPERIOR HEMORRHAGIC POLIOENCEPHALITIS (WERNICKE)

Wernicke's disease (acute superior hemorrhagic polioencephalitis) is probably due to *deficiency of thiamine chloride and niacin* (p 623) Often it is associated with *chronic alcoholism* (p 3851) which clouds the clinical manifestations

The onset of Wernicke s disease may be acute or gradual with head ache nausea vomiting insomnia or somnolence and diplopia Examina tion reveals nystagmus partial or complete internal and external ophthal moplegia rigidity of the extremities abnormal posture and abnormal movements suggesting disturbances in the basal ganglia The sleep rhythm is disturbed and there may be insomnia somnolence or coma

TABLE 100 —THE SCLEROSES

Type	Age	Site of Pathologic Lesion	Clinical Manifestations
Subacute Combined Sclerosis	Middle age	Posterior horns posterior columns pyramidal tract	Spastic paralysis Tabetic syndrome
Amyotrophic Lateral Sclerosis	35–40	Anterior horns pyramidal tract	Atrophies especially of hands Spastic paralysis Bilateral and symmetrical involvement
Primary Lateral Sclerosis	Any age	Pyramidal tract	Spasticity Weakness
Progressive Bulbar Palsy	Older patients	Medulla Pons Bulb	Dysarthria Dysphagia Cranial nerve palsies Dysphonia Nasal voice
Multiple Disseminated Sclerosis	Young	Widespread with remissions and exacerbations	Diplopia Nystagmus Dysphonia (scanning speech) Ataxia Tremor Spastic Temporal pallor of opti disk
Syringomyelia	Any age	Central gliosis	Dissociation on sensory s de with loss of pain and temperature contralaterally and touch anesthesia ipsilaterally Later pyramidal tract spasticity
Syringobulbia	Any age	Central gliosis	As above but with associated cranial nerve involvements and bulbar signs

Wernicke s disease is best treated by intravenous injections of large doses of *thiamine chloride* and *niacin* Recovery takes place in several weeks but recurrences are to be expected if alcoholism continues

intravenous injections of histamine phosphate using 2 75 mg in 250 cc of isotonic saline at a rate of 2 0 to 6 0 cc per minute High vitamin *diets* are employed and accessory multivitamin preparations are administered No consistent beneficial effects have followed treatment with heparin (p 1050) dicoumarol (p 1049) hyperpyrexia (p 1379) quinine (p 516) liver extracts (p 1048) or deleading (p 764)

SYRINGOMYELIA

Syringomyelia is a degenerative disease of the spinal cord in which the predominant pathologic lesions are in or near the central canal (*status dysraphicus*) The lesion causes a disruption of function affecting the mid line structures of the body and central nervous system It may be that fundamentally there are *inclusion rests* along the line of closure of the neural tube and when these later proliferate and degenerate they produce local or diffuse degeneration and cyst formation in the cord and brain stem With syringomyelia there are often other associated midline *congenital defects* such as spina bifida improper closure of the cervical vertebrae supernumerary ribs and congenital anomalies of the hands feet and ears At times there is a proliferation of astrocytes about the central gliosis suggesting a new growth

Clinical Manifestations—The clinical manifestations of syringomyelia result from interruption of the crossing spinothalamic fibers There is diminution in the *pain* and *temperature* senses so that the patient develops *burns* and *trophic ulcerations* in the regions of the lesion *Morvan's disease* is a subvariety of syringomyelia in which there are ulcerations of the finger tips multiple paronychia and sensory changes With later progression *there is pyramidal tract involvement with spastic weaknesses* of legs and arms The sensory manifestations are contralateral whereas the motor disturbances are ipsilateral

Treatment—Syringomyelia is treated by *roentgen therapy* Occasionally evacuation of a single large intramedullary cyst is associated with some transitory improvement

SYRINGOBULBIA

Syringobulbia *is a syndrome resembling syringomyelia (p 1505)* except that there are involvements of the upper cord medulla and the cranial nerves Fibrillations atrophies and paralyses are noted in the tongue palate uvula and vocal cords Sensory changes are apparent in the regions innervated by the trigeminus with a crossed sensory dissociation

PARALYSIS AGITANS (SHAKING PALSY PARKINSON S DISEASE)

Paralysis agitans is a chronic affection of the central nervous system in which there is primary atrophy of the *striopallidal systems* Paralysis agitans has a definite familial and hereditary trend and is twice as common in men as in women It is characterized by *progressive weakness muscle rigidity* and *tremor* In older patients the disturbance is often on an *arteriosclerotic basis* but it may be neoplastic Juvenile and presenile types follow *epidemic encephalitis* (p 441) and may be associated with *exophthalmos* and signs of *hyperthyroidism* (p 1107)

ness spasticity exaggeration of tendon reflexes and a chronic course that may last many years Most often, the patient presents a *spastic paraplegia* with a 'scissors gait There are no sensory disturbances and pain does not occur

Treatment has been attempted surgically by division of posterior roots with inconsistent results

Progressive Bulbar Palsy

Progressive bulbar palsy is a rare disease of older people in which there are difficulties in speech swallowing mastication and phonation due to atrophy of the muscles of the lips tongue palate pharynx and larynx The disturbance is a degeneration of the cells of the *motor cranial nerves* situated in the *pons* and *medulla* It is probably the same disease as *amyotrophic lateral sclerosis* (p 1503) except for the site of the disturbance The etiology is unknown and pathological examinations show *degenerations of the motor nuclei of XII XI, IX VII and V*

The *clinical manifestations* include difficulties in articulation in puckering the lips as in whistling and in speaking and swallowing The voice assumes a nasal character it is difficult to protrude the tongue which shows fibrillary tremors mastication and deglutition are impaired aspiration into the larynx may produce a pneumonitis The symptoms gradually increase for a few years after which death occurs from inanition There is no successful form of therapy

Multiple Sclerosis (Disseminated Sclerosis)

Multiple sclerosis represents a process of *demyelination* and seems to be increasingly prevalent Its etiology is unknown and the fundamental pathologic change seems to be a thrombosis of the local vessels causing areas of degeneration Present investigations are concerned with a possible relationship to *hemorrhagic diathesis* (p 1108) and the various forms of *endophlebitis*

Clinical Manifestations —Multiple sclerosis is a disease of *early adult life* and occurs equally in males and females Occasionally it seems to follow an acute infection The clinical manifestations of multiple sclerosis cover the entire range of neurology and psychiatry depending upon the area involved Frequent signs include transitory *double vision unsteadiness of an arm or leg tremor* and *disturbances of the bladder or bowel* with complete clearing in a few hours a few days or a few weeks The involvement is usually patchy and it is impossible to explain the findings on the basis of a single lesion such as might be present with a neoplasm (p 1430)

Course and Treatment —The course of the disease is characterized by *remissions* and *exacerbations* each acute episode is followed by some progressive secondary degeneration of the axis cylinder There is a steady increase in the amount of permanent damage to the nervous system with characteristic manifestations of pyramidal tract involvement causing *spasticity Disturbances of speech* are common as are *oculomotor palsies* and *nystagmus* The course of the disease is prolonged and the amount of incapacitation may be minor or major

Somewhat encouraging therapeutic results have followed repeated daily

often in sedentary and intellectual persons between the ages of sixteen and fifty The origin of the disturbance is unknown but precipitating causes are often clearly demonstrable

Aura—The migrainous headache is usually preceded by an aura This phenomenon has importance since it links the affliction to *epilepsy* (p 1515) and also serves as a herald manifestation to initiate preventive treatment (p 1508)

The aura though protean in its manifestations is usually distinct for each individual It may consist of irritability nervousness photophobia vomiting constipation an attack of diarrhea intestinal spasmosis scotomas hemianopsia lid lag paresthesias abdominal distention a sudden feeling of chilliness or flushing vertigo tremor sweating an aphasia or coldness of the extremities Sometimes the aura is recognized by the husband or wife who observes a change in disposition or a facial expression of tenseness Often the patient is not aware of the aura unless the physician urges concentration on the prodromal manifestations

Cephalalgia (Hemicrania)—The headache of migraine like the aura is usually individual It usually comes on at a *definite time* in the course of the day Morning afternoon and evening types are recognized Occasionally the headache bears a relationship to the *day of the week* Sunday headaches are observed in those who find difficulty in relaxing on the Sabbath Monday headaches are noted in those who overeat on the day of rest and have difficulty in overcoming their inertia for the beginning of the next week *Premenstrual menstrual postmenstrual* and *ovulation attacks* are observed in women who often note relief with the onset of menopause

The headache may be a complete hemicrania it may be orbital frontal temporal parietal occipital or referred down the neck and into the shoulders The description of the pain may be dull throbbing pulsating bursting or agonizing or there may be merely a feeling of fullness

Digestive Disturbances—The headache is almost invariably accompanied by gastro-intestinal manifestations such as anorexia a bad taste in the mouth a bad odor to the breath nausea vomiting spastic constipation or diarrhea Occasionally the gastro-intestinal symptoms are prodromal and the patient recognizes from the change in the character of the stool that a headache is imminent

Other Disturbances—At times the headache is associated with *ocular phenomena* such as a lid lag scintillating scotomas amaurosis hemianopsia or an ophthalmoplegia Photophobia is very common and few patients can stand exposure to bright or even normal light An *eosinophilia* occasionally is noted suggesting an *allergic element* in the disturbance (p 547)

Vasomotor phenomena usually accompany the headache The extremities become cold and clammy there may be flushing or blanching of the face and often the pulse rate slows perceptibly from vagal stimulation

Postmigrainous Euphoria—Following the migrainous headache there occur a sense of relief and a feeling of relaxation that borders on elation Cerebration is alert and crystal clear and this seems the 'best of possible worlds

Course—The course of the migrainous headache follows a unique and individual pattern It usually lasts for just so long and then disappears

Clinical Manifestations—The onset of paralysis agitans is insidious and the progress is slow and gradual The herald symptom is the appearance of a fine *rhythmic tremor* involving the index finger and thumb *Weakness* and *stiffness* are noted in the movements of the digits and soon the rigidity and adynamia increase in extent and severity until the entire body is involved

Tremor—The tremor is rhythmic, occurs at a rate of four to seven vibrations per second and has a characteristic *pill-rolling movement* It disappears during sleep and is brought out by voluntary movements best illustrated by having the patient attempt to drink a tumblerful of water

Rigidity—The rigidity is noted in the extremity musculature but also produces a *masklike facies* Winking is uncommon a generalized attitude of flexion is observed with the thumb turned into the palm the fingers flexed into a fist the neck depressed on the chest and the spine curved into a permanent kyphosis

Gait—A characteristic of paralysis agitans is the *propulsion gait* The steps are short and there is a tendency to *festination* until the patient finds himself running and can only stay his progress by bumping into an immovable object During walking the arms are held stiffly at the sides and they do not swing in the normal manner

Miscellany—Paralysis agitans is not associated with any significant changes in the reflexes sensorium or visceral functions There may be a slight *elevation in temperature* a tendency to *hyperidrosis* and *sialorrhea* Intelligence is not affected to the extent that might be anticipated by the stupid expression of the face

Treatment—The treatment of paralysis agitans is essentially symptomatic The patient may live for many years and die of some intercurrent condition The tremor may be well controlled by *belladonna* and similar preparations The oral use of *stramonium* (p 3875) in doses of 0 16 gm (2½ grains) four times daily has its adherents Drop doses of *tincture of belladonna* (p 3875) are recommended and emphasis has been placed on a *Bulgarian root* which is said to have greater potency than those of native habitat Commercial preparations such as *bellabulgara* and *rabellon* have had wide publicity, our best success has been with injections of *hyoscine hydrobromide* (p 3875) As little as 0.2 mg (1/300 grain), given subcutaneously may afford relief for several hours so that only two or three injections are needed daily for comparative comfort A member of the household may be entrusted to give the injections since self medication is prevented by the tremor

The combination of *belladonna* and *amphetamine sulfate* (benzedrine) seems particularly helpful in postencephalitic Parkinsonism especially in patients with oculogyric crises

MIGRAINE

Migraine is one of the varieties of *headache* (p 1510) Although the term often is used loosely as a synonym for headache it constitutes a definitive clinical entity that occurs only in a small per cent of the total number of cephalalgias

Clinical Manifestations—The typical migrainous headache is a *periodic hemicrania* Attacks are usually *familial* and *hereditary* They occur more

ANTIHISTAMINES.—The successful introductions of antihistamines affords a fresh and hopeful approach to the management of migraine. Both for prevention and therapy, pyribenzamine (p 665) may be given in doses of 50 to 100 mg every two to four hours for at least six doses.

OXYGEN THERAPY.—Inhalations of oxygen give occasional relief to the migrainous headache. The method is worthy of trial if a tank and a mask are available.

ERGOTAMINE.—*Concurrently* with the use of the analgesic *ergotamine tartrate* marketed as *Gynergen* (p 3833) or dihydro ergotamine is given subcutaneously in a dose of 1 mg (1/60 grain) or intravenously in the amount of 0.4 mg (1/150 grain). The initial injection of Gynergen is given by the physician at his office. The patient remains under observation for at least an hour to note any *idiosyncrasy* such as nausea, vomiting, paresthesias and angiospasms of the extremities. The drug is withheld *in pregnancy, in patients with significant arteriosclerosis, hypertension, angina, or Raynaud's disease.*

In the absence of untoward manifestations the patient is taught to self administer the drug by hypodermic and the dose is regulated according to the individual needs.

THIAMINE CHLORIDE.—The treatment of migraine has been advanced also by the use of intravenous injections of 100 to 200 mg (1½ to 3 grains) of *thiamine chloride* (p 622). These are given *in addition to the headache remedy and the Gynergen.*

MISCELLANY.—An occasional patient reports relief by the use of *pressure* to "trigger points" such as the regions of the temporal or occipital foramina. These maneuvers emphasize the possible pathogenesis of a migrainous headache as a distention of the relaxed walls of the cranial arteries. An *ice cap* to the head is often grateful though some patients prefer *heat*. *A scalp rub with 0.5 per cent menthol in alcohol or with a menthol stick* ("headache pencil") *sometimes gives* a measure of comfort.

Other infrequently applied and not consistently useful agents include injections of hypertonic salt solutions, the pituitary extracts or caffeine. Inhalations of *nitroglycerine* have been advised but our experiences emphasize the greater likelihood of increase in the headache after temporary relief. Attempted vasoconstriction by the uses of *ephedrine* or *amphetamine (benzedrine) has met with no consistent benefits in our experiences.*

Injections of potentially habit forming drugs are reserved for dire occasions. Demerol, codeine, dilaudid and morphine are withheld if it is at all possible.

Internal Treatment.—After an attack most patients are eager for prophylactic therapy of any sort. General instruction is given in *personal hygiene* with particular reference to working hours, reading *habits*, the use of the eyes, the care of the bowels, an abundance of outdoor exercise and longer hours of sleep. Often a *holiday* is followed by considerable surcease (p 3761). The *nasal accessory sinuses* are investigated and any inflammatory process is eradicated if possible. The *teeth* are carefully examined *and possible foci of infection* are eliminated. There is always a vogue for *colon irrigations* and many patients *testify to their* usefulness. A *saline purge* taken each Sunday probably fulfils the same purpose at lesser trouble and expense.

The duration may be several hours or several days Repetitions may be frequent or unusual An associated *epilepsy* (p 1515) occurs in a ratio that is disproportionately high in reference to the general population

Treatment —In the management of migraine the aim of the therapeutist is the prevention of the recurrence of attacks In the event of failure, the individual headache requires symptomatic attention

Prophylaxis —Since each migrainous sufferer presents a unique problem it is good practice to request the patient to keep a 'diary history' (p 3474) Many interesting clues are obtained which have important bearing on the prevention of attacks Certain of the more common *precipitating circumstances* include emotional strain constipation, eating before bedtime exposure to special foods such as milk chocolate eggs pork nuts cauliflower tomato, or cabbage excessive smoking, the particular use of cigar or pipe a delayed bowel movement, fatigue alteration in the daily routine such as eating the heavy meal in the middle of the day on Sunday excessive use of alcohol in any form or of some particular brand such as gin rum brandy, or a mixture of drinks, menstruation or ovulation, excessive indulgence in sexual intercourse, prolonged periods of sexual continence eyestrain due to reading in bed until the late hours of the night, imperfect illumination and excessive purging

The study of the diary assists greatly in spacing out and perhaps preventing the onset of the migraine It has value too in the attempt to abort an attack, upon recognition of the aura

Abortive Treatment —The use of the diary history enables the patient to recognize the individual pattern of the aura The value of active treatment during this period far transcends that of measures employed once the headache has begun Perhaps the greatest single effectual effort is *evacuation of the bowels* by the use of an *enema* or a *saline purge* Each sufferer from migraine agrees on the value of rest in a darkened room If it is at all convenient a *warm relaxation bath* is taken and the affluent find comfort in *massage* (p 3766) The oral use of *calcium lactate* in doses of 2 gm (30 grains) every two hours and inhalations of 100 per cent *oxygen* are successfully employed by some sufferers Active treatment with drugs is vigorously initiated, as outlined in the next paragraph rather than procrastination until the headache begins

Active Treatment —If abortive treatment has not been initiated the measures previously described are started at the onset of the headache

THE HEADACHE CAPSULE' —The headache capsule is taken orally and washed down with a *caffeinated beverage* such as coffee tea or a cola drink

℞ Acetylsalicylic acid	5 0
Acetphenetidin	4 75
Phenobarbital	0 25
Divide	
Ft Caps or Powders No 15	
Sig. One hourly for 3 doses	

or

℞ Acetylsalicylic acid	4 5
Codeine phosphate	0 5
Divide	
Ft Caps No 15	
Sig One hourly for 3 doses	

insensitive to pain Only in the vicinity of large vessels are *dura* and *arachnoid* responsive to painful stimuli Thus the actual site for the pro duction of the sensation of pain in the head is narrowed to the vessels which may be altered by vasoconstriction vasodilatation or stretching

The importance of vascular elements in the pathogenesis of headache is emphasized by the effects noted with drugs whose action is on the per ipheral vascular musculature Thus headache may be produced by *epi nephrine* which elevates blood pressure through vasoconstriction and by *nitrites* and *histamine* which rapidly lower vascular tension by producing widespread vasodilatation

Clinical experience points to the importance of disturbances in spinal fluid pressure relationships Lumbar puncture with withdrawal of spinal fluid is often but not invariably associated with headache Headache also *occurs when air is injected into the ventricles in the course of diagnostic* pneumoencephalography

Despite the production of headache by disturbances in pressure rela tionships the majority of complaints as ordinarily seen are unaccom *panied by definite alteration The practitioner is therefore reduced to in* terpreting the derangement as a manifestation of toxemia Some of the toxic processes are capable of tangible definition as in the instance of head aches that accompany anoxemia acute anemia acidosis dehydration and water intoxication In certain examples of migraine occurring near the time of the menses there seems to be an excess of gonadotropic hormone in the urine with a deficiency of estrogen suggesting a hormonal imbal ance as the provocative factor in the disturbance

In the majority of clinical experiences unfortunately the toxic factor is not demonstrable Those who enjoy speculation concerning medical prob lems hypothesize the release of histamine like substances from the bowel or of internal urticarial lesions within the confines of the cranium

Types of Headache and Their Management —The management of acute or recurrent headache may be facilitated by attention to the following de tails regarding the type of headache

1 —*Frontal and supra-orbital headache* is more common with sinu sitis intranasal disturbances and trigeminal neuralgia involv ing the ophthalmic branch

2 —*Unilateral temporal headaches* suggest migraine or temporal ar teritis They also occur with disturbances of the eye and ear

3 —*Facial pain* may be due to involvement of the antra or of the trigeminal or sphenopalatine nerve elements

4 —*Occipital pain* occurs in spheno ethmoiditis hypertension eye strain chronic nephritis meningitis indurated myositis (nod ular headache) and cervical occipital neuralgia

5 —The *vertex headache* is probably hysterical

6 —*Pounding headache* occurs more often with migraine than hyper tension

7 —The etiology of *recurrent headache* is often best elucidated by the *diary history with particular emphasis upon overeating* over drinking oversmoking excessive indulgence in candy choco late or starches constipation fatigue mental or emotional strain or stress insomnia excessive use of coffee or tea poor

Those who favor the allergic aspect of migraine practice *desensitization injections* of *proteoses* and *peptones* Multiple *skin tests* are performed and suspicious substances are forbidden in the diet *Elimination regimens* (p 562) are often utilized with some measure of success The students of metabolism advocate the use of *ketogenic diets* (p 675) but these are impracticable for prolonged use Probably an analogous effect may be obtained with less nuisance by administering 6 to 8 gm of *ammonium chloride* daily for three to four days at the expected time of the headache Pyribenzamine (p 565) should be continued intermittently

Enthusiasts for *hormone therapy* point to the increased excretion of *prolan* in the urine at the time of the headache and to the relationship that is often demonstrable between ovulation menstrual cycle and attacks We are not averse to injections of *anterior pituitary extracts* (p 1154) for a limited probatory period, but we entertain a healthy respect for the side effects which may be associated with the uses of *androgen* and *estrogen* The former is capable of resulting in sexual impotence in the male and may postpone menstruation and cause the appearance of male secondary sexual characteristics in the female (p 2515) Estrogen has carcinogenic potentialities which menace the peace of mind of conservative practitioners such as the senior author

Useless Measures—The long list of useless measures includes desensitization with histamine the administration of histaminase (torantil), Veratrum viride Gelsemium Cannabis indica and surgical procedures such as tonsillectomy appendectomy cholecystectomy corrections of uterine malposition perineal repairs resections of the large bowel or the roots of the fifth cranial nerve

HISTAMINE CEPHALALGIA

Histamine cephalalgia is thought to be a form of unilateral headache that is distinct from migraine It is of brief duration and is associated with *tearing* and *vasomotor rhinitis* on the affected side It is reproduced by injections of *histamine* and may be controlled by anti histamine drugs particularly pyribenzamine (p 565) in doses of 50 to 100 mg

THE GENERAL MANAGEMENT OF HEADACHE

Headache is a common presenting symptom For every one concerning which the physician is consulted however countless headaches occur for which the patient practices self medication with popularly advertised home remedies

The Mechanism of Headache.—Despite the frequent occurrence of headache there is limited knowledge concerning its mechanisms Clinical data relate to observations concerning the sensitivity of cranial and intracranial structures as observed under local anesthesia the effect of drugs which alter blood pressure the results of alterations in spinal fluid pressure relationships and problems of toxemia

The neurosurgeon operating under local anesthesia notes that dura arachnoid pia cerebral tissues choroid and ventricular ependyma are

insensitive to pain Only in the vicinity of large vessels are *dura* and *arachnoid* responsive to painful stimuli Thus the actual site for the production of the sensation of pain in the head is narrowed to the vessels which may be altered by vasoconstriction vasodilatation or stretching

The importance of vascular elements in the pathogenesis of headache is emphasized by the effects noted with drugs whose action is on the peripheral vascular musculature Thus headache may be produced by *epinephrine* which elevates blood pressure through vasoconstriction and by *nitrites* and *histamine* which rapidly lower vascular tension by producing widespread vasodilatation

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DIFFERENTIAL DIAGNOSIS OF

Headache

Lacking a clearcut conception of the toxic factor operative in most cases of headache and of the mechanisms by which noxious elements operate the practitioner is dependent upon his clinical acumen in elucidating the problems of headache In the majority of instances, his great reliance is placed upon the accuracy and care with which he collects and evaluates the material of the history and the thoroughness with which he undertakes the physical examination

CAUSE	DIAGNOSTIC FEATURES
Errors in Hygiene	Excitement anxiety constipation gluttony excessive fatigue Indulgence in alcohol overheating insolation, excessive smoking Idiosyncrasy to chocolates starch, candy or eggs. The wearing of a tight hat band Poor ventilation insomnia excessive noise overbright or poor illumination Check history
Pharmacologic	From epinephrine nitrite histamine caffeine opiate general anesthetics hypnotics iodids, salicylates quinine quinidine or sulfonamides Following spinal or caudal anesthesia Check history
Toxic	Overdoses of the drugs above mentioned Fumes in industry Jaundice
Metabolic	Anoxemia dehydration acidosis cholemia, premenstrual or menstrual tension, renal insufficiency azotemia methemoglobinemia, hypoglycemia fever allergies hyperpituitarism and auto-intoxication Urinalysis and blood chemistry (p 3712)
Hemic	Anemia and polycythemia Obtain hemogram (p 3704)
Circulatory (Systemic)	Hypertension and hypotension Particularly with hypertensive toxemia of pregnancy and malignant phase of hypertension (p 916) With forward and backward failure (p 941)
Neurocirculatory	Angiospasms Cerebral arteriosclerosis embolization or thrombosis With increased intracranial tension In temporal arteritis With cerebral accidents such as rupture of an aneurysm of the circle of Willis and subarachnoid or interventricular hemorrhage With edema of the brain
Infections (Generalized)	Particularly with influenza typhoid, typhus spotted fever tuberculosis brucellosis, secondary syphilis relapsing fevers dengue measles meningococcemia yellow fever infectious jaundice malaria and infectious mononucleosis
Infections (Neurologic)	Nonsuppurative encephalitides Brain abscess Meningitides Poliomyelitis Check spinal fluid (p 3734) Temporal arteritis (p 1037)
Neuroses	With anxieties hysteria (clavus) neurasthenia and hypochondriasis Malingering
Psychoses	General paresis and cerebrospinal syphilis Check spinal fluid (p 3734)

Neurogenic	Migraine (p 1506) Epilepsy (p 1515) Trigeminal sphenopalatine or occipital neuralgia (p 1482) Hydrocephalus (p 1409) Get x rays electrocardiogram, and check spinal fluid
Osseous	Osteomyelitis and gummas of the skull Following trauma concussion or fracture With osteitis deformans, multiple myeloma and skeletal metastases Get x rays
Skeletal	Cervical spondylitis and occipital myositis or fibrositis Take x rays of spine
Respiratory	With upper respiratory infection, nasal obstruction, pansinusitis spheno-ethmoiditis and Sluder's syndrome Get x rays of sinuses Refer to specialist for lavage of antrum and cocainization of ganglion
Ophthalmic	With eye strain, conjunctivitis iritis keratitis retinitis orbital cellulitis and glaucoma Refer to specialist
Otogenic	With otitis media, labyrinthitis mastoiditis and petrositis Refer to specialist

ventilation in the bedroom or the workshop the inhalation of noxious fumes in industry eye strain excessive noise or lighting insufficient illumination the onset of menstruation the habitual use of drugs such as narcotics hypnotics analgesics and sulfonamides exposure to sun

8 —A *band headache* usually characterizes fatigue

9 —A *hammering headache* is often of hysterical origin

10 —The headache that is *worse in the morning* is often due to sinusitis or alcoholism

11 —The headache that *is worse at night is often due to intracranial* disease osteomyelitis of the skull nephritis or eye strain

12 —*Recurrent headaches with a definite pattern* are almost invariably of migrainous origin

13 —The *Sunday morning headache* is either migrainous or a hang over of the Saturday night debauch

14 —The *Monday morning headache* is usually due to malingering

15 —*Cyclic headaches* which occur intermenstrually premenstrually or menstrually are often due to disturbances of water metabolism and are relieved by ammonium chloride diuresis (p 614)

16 —*Relief* of headache following an *enema* or a *purge* suggests the factor of auto intoxication

17 —*Relief* of headache following an *analgesic antipyretic* such as acetosalicylic acid 0 3 gm (5 grains) suggests that the headache is *of casual* and minor importance

18 —*Relief* of headache following the injection of 0 5 to 1 mg ($\frac{1}{120}$ to $\frac{1}{60}$ grain) of *ergotamine tartrate* suggests that the headache is of migrainous origin

19 —*Exacerbation* of headache when the *head is bent* over or *shaken* suggests sinusitis

20 —In *febrile headache of recent origin* the nose nasal accessory sinuses and spinal fluid warrant investigation

21 —With headache in *association with eye or ear disorders* specialist consultation is mandatory

22 —Except for the headache of the hypertensive toxemia of pregnancy and malignant hypertension in the young and middle aged *elevation of blood pressure* is usually an accompaniment and not a cause of headache

23 —Except in marked degrees of hypotension *lowering of blood pressure* is usually an accompaniment and not a cause of headache

24 —Except in profound or acute anemia a *blood disturbance* is rarely a cause of headache

25 —Except in marked polycythemia a blood disturbance is usually an accompaniment and not a cause for headache

26 —*Neuralgias* of the *trigeminus* and *sphenopalatine elements* yield to local cocainization or alcohol injection

27 —Headache *accompanied by flushing of the face lacrimation* and *acute swelling of the nasal mucous membrane* occurs with the histamine variety of the complaint

28 —*Skull tenderness* may be demonstrated over the brain abscess or brain tumor

29 —*Sinus tenderness* is particularly acute in recent infections

30 —The *points of emergence* of the branches of the trigeminal nerve are exquisitely tender in the neuralgias

31 —*Mastoid tenderness* is of grave significance in ear infection

32 —Thickening of the insertion of the heavy muscles into the occiput suggests the *nodular type of headache* due to an indurative myositis

33 —Lavage of the nasal accessory sinuses and radiographs are indicated if there is *obstruction to the airway nasal* or *post nasal discharge* a *history of recent cold congestion or swelling of the turbinates nasal polyps* or deficiencies in *transillumination*

34 —*Hardening of the eye balls* with intense headache suggests glaucoma and calls for the prompt use of miotics (p 1548)

35 —*Examination of the fundus oculi* should be a routine procedure in the investigation of any headache

36 —*Inspection of the ear drums* should be routine in unilateral headaches particularly in infancy and childhood

37 —With febrile headache *rigidity of the neck* should be sought Lumbar puncture is performed if there is any suspicion of difficulty

38 —A *routine urinalysis* is required in the investigation of all headaches Pertinent findings include fixation of the specific gravity albuminuria glycosuria, acetonuria and indicanuria

39 —A *routine blood count* is required in the investigation of the more persistent and severe grades of headache Anemia polycythemia and leukocytosis merit further investigation

40 —*Pertinent blood chemical findings* include hypoglycemia hyperglycemia azotemia cholemia and methemoglobinemia

41 —A *neurological status examination* is required in all persistent or recurrent headaches

42 —*Psychiatric investigation* is merited if there is a suspicion of hysteria

43—*X-ray of the skull* is necessary if there is any history of preceding trauma or any compensation factor

44—*Indurative headache* is often relieved by local massage

EPILEPSY

It is conservatively estimated that there are one half million epileptics in the United States The syndrome of *idiopathic epilepsy* which is differentiated from *symptomatic epilepsy* such as occurs with brain tumor is best described as a paroxysmal cerebral dysrhythmia

Etiology—Epilepsy is a *familial disease* in 20 per cent of patients It may be related to birth traumas intracranial pathology and migraine *Like the latter it is probably a metabolic disorder with the sudden liberation of some endogenous toxin*

The Epileptic Constitution—The epileptic constitution is clearly recognized Most patients are gloomy easily irritated suspicious emotionally impoverished as best illustrated by the monotony of their conversation and their conversational tone quarrelsome hypersensitive subject to violent rages somewhat paranoic sulky and disagreeable It is difficult to *determine how much is part of the epilepsy and what portion results* from the knowledge and fear of the seizures

Many epileptics remain mentally normal Others deteriorate partially as the result of the disease but mostly from the injudicious use of bromides and alcohol and the psychological implications of their affliction

Clinical Manifestations—The clinical manifestations of epilepsy are characterized by an *aura* a *convulsive stage* (*grand mal*) and a *postepileptic phase* The convulsive stage may be replaced by a *petit mal* or a *psychic equivalent*

The Aura—The aura of epilepsy like that of migraine is individual and characteristic It may consist of some optic olfactory gustatory motor sensory emotional or characterological disturbance The observant patient *will almost invariably recognize the prodrome which may be apparent also* to a mother a husband or a wife

Convulsion—The epileptic convulsion is characterized by *loss of consciousness* and a *falling to the ground* There is often an eerie and ominous *cry* The convulsion is *tonic* at first but later becomes *clonic* and is often associated with *involuntary urination* and/or *defecation* At times there is *erection* with *ejaculation* in males

During the convulsive period *the face becomes ashen and then cyanotic* due to breath holding The tongue is bitten and there is foaming at the mouth The pupils are usually miotic at first but later they become mydriatic During the tonic and clonic phases respiration may be slowed or a period of complete apnea is observed At this time the pulse becomes almost *imperceptible*

Petit Mal—The convulsive form of grand mal of epilepsy is sometimes replaced by petit mal characterized by transitory *loss of consciousness* The attack may be so fleeting that the patient is unaware of its existence Observers note a blankness of expression a rolling of the eyes or a sudden *drooping of the head The patient has an amnesia* during the period of attack and goes on with conversation and activity as if nothing had happened These attacks of petit mal are particularly dangerous since the sub

ject may suffer injury to himself during the period of unconsciousness or he may inflict grave damage to others if, for example he is driving a motor car or working with machinery

Psychic Equivalents —Psychic equivalents occur in epileptics in place of the attacks of grand or petit mal The individual becomes manic irate homicidal exhibitionistic or perverse In children, the affliction may be mistaken for inexplicable naughtiness At times the equivalent is accompanied by muscle twitching blinking word perseveration or other forms of automatism (p 1308) Associated attacks of migraine occur with undue frequency

Status Epilepticus —The most violent type of epilepsy is that in which there are rapidly recurring attacks (status epilepticus) These may be accompanied by stupor, hyperpyrexia circulatory failure coma and even death

Postepileptic Phenomena —Following the grand mal particularly post epileptic phenomena are noted They may consist of stupor sleep automatism amnesia and particularly headache Some patients become aware of an attack only through the development of cephalalgia or the appearance of a bitten tongue Following epilepsy there may be a period of automatism in which irrational and even criminal acts of violence are performed The latter have medicolegal significance

Diagnosis —The diagnosis of epilepsy was formerly based on clinical manifestations The introduction of *electro encephalography* (p 1403) permits curves to be presented illustrating grand and petit mal and the psychic equivalents When possible the practitioner should refer his patient to the expert for this information in the manner in which he obtains an electrocardiogram in the patient with circulatory disease although all epileptics do not show abnormal graphs

Despite electro encephalography the diagnosis of idiopathic epilepsy is best made by exclusion A careful *neurologic status* is conducted relative to motor sensory and reflex phenomena *A film of the skull* is required and the *spinal fluid* is examined cytologically serologically and by the colloidal gold curves The *optic nerve head* is viewed by the ophthalmoscope and the *visual fields* are plotted to detect defects

When there is doubt concerning the diagnosis of epilepsy the water pitressin test may be employed Anticonvulsive medication is avoided for twenty-four hours prior to the test The patient is kept in bed on a normal diet throughout the test and for an additional twenty four hours, at hourly intervals when the test is started a pint of water is ingested starting with the fourth pint of water pituitrin is given hourly in doses of 0 2 0.3 0 4 0 5 0.5 0.5 0.5 and 0 5 cc the fluid intake and output are charted and the blood pressure is recorded hourly

In the positive test a convulsion is induced in more than 40 per cent of those who suffer from true epilepsy The test is discontinued with the appearance of severe headache gastro intestinal distress elevation of blood pressure or the actual convulsion

The presence of any positive finding demands specialist consultation for an investigation of organic intracranial disease such as neoplasm infection a vascular accident or an unsuspected fracture Pneumencephalography is required when focal signs or focal seizures are present

Treatment—The treatment of epilepsy follows the plan employed in migraine (p 1508) A *diary* is kept to reveal precipitating circumstances *Efforts are made to prevent the seizure since little can be done once the attack has started*

Prevention—Attempts are made to prevent attacks of epilepsy by general measures of hygiene The errors that must be avoided include over eating overdrinking fatigue emotional disturbances constipation excessive sexual intercourse excessively prolonged sexual continence and the abuse of alcohol or tobacco

DIETOTHERAPY—Prophylactic dietotherapy in the management of epilepsy consists of the use of a *ketogenic routine* (p 675) *This is distinctly* an institutional procedure and of temporary value in patients who are having repeated or severe attacks Perhaps the same purpose can be accomplished *by the generous administration of acidifying salts such as ammonium chloride* 6 to 8 gm daily for three days on and two days off

PHARMACOTHERAPY—Useful drugs include tridione phenobarbital and dilantin Tridione (3 5 5 trimethyloxazolidine 2 4 dione) is dispensed in capsules containing 0.32 gm (5 grains) Its daily dose is from 1 0 to 2 0 gm irrespective of age Tridione is of particular value in treating seizures with divergent clinical appearances pykno epilepsy and myoclonic and akinetic attacks Aplastic anemia and agranulocytosis have followed tridione administration

Many epileptics are quite completely controlled by *phenobarbital* given in amounts of 0 06 to 0 13 gm (1 to 2 grains) daily Except for a rare eruption phenobarbital has no significant untoward effects and the results have been quite satisfactory Dilantin given in doses of 0 1 gm (1½ grains) three times daily has proven even more effective than phenobarbital with which it can be alternated or combined Dilantin has the disadvantage of causing more frequent untoward symptoms such as nausea *vomiting substernal burning bleeding of the gums stiffness tremor* ataxia and a generalized eruption The hemorrhagic tendency may be prevented by the simultaneous administration of *cevitamic acid* (p 629) Unlike phenobarbital dilantin does not cause any depression and has proven a tremendous addition to the armamentarium of epilepsy

More recent innovations in the therapy of epilepsy are glutamic acid and mebaral Mebaral known in Europe as prominal is methylethyl phenylbarbituric acid It is dispensed in tablets of 0 2 gm (3 grains) and *the average dose is 1 tablet two or three times daily* Mebaral may be substituted for phenobarbital but the changeover should be gradual increasing the dose of the mebaral as the phenobarbital dose is decreased and then discontinued

COMBINATION THERAPY—A combination form of prophylactic therapy *in epilepsy is suggested as undernoted*

1 Accomplish *dehydration* once weekly by limitation of fluids to 600 cc and the use of a saline purge
2 Produce a therapeutic acidosis *two or three days weekly* by administering *ammonium or calcium chloride* in doses of 6 to 8 gm using capsules containing 0 5 gm
3 For the first half of each month give *phenobarbital* in the dosage of 0 06 to 0 13 mg (1 to 2 grains) daily and during the last half

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are paroxysmal are described as *clonic* whereas maintained movements are of a *tonic* character

Treatment of Convulsions —It is the obligation of the practitioner to protect the patient during the convulsive seizure Afterward diagnostic in

DIFFERENTIAL DIAGNOSIS OF

Convulsions

Generalized convulsions have less diagnostic significance than focal or Jacksonian seizures which indicate a fairly localized lesion. Most convulsions are associated with unconsciousness, amnesia and loss of sphincteric control The most frequent cause for repeated convulsive episodes is idiopathic epilepsy

CAUSE	DIAGNOSTIC FEATURES
Infectious	Nonspecific manifestation of acute invasion *particularly in infancy and childhood.* With encephalitides (p 1463) meningitides (p 1462) and tetanus (p 294) Check spinal fluid.
Metabolic	Hyperpyrexia particularly in infancy and childhood. Tetany and rickets. Alkalosis and hypocalcemia Diabetic coma and hypoglycemia Uremia, azotemia and renal insufficiency Cholemia Anoxemia and asphyxia Addisonian crises (p 1275) Obtain urine and check blood chemistry
Neurogenic	Epilepsy (p 1515) Following trauma particularly to the skull With local infection such as encephalitis poliomyelitis meningitis rabies *tuberculous meningitis general paresis syphilitic* meningo-encephalitis brain abscess and lateral sinus thrombosis (p 1446) With hydrocephalus tuberous sclerosis and idiocy With brain neoplasms and cysts Supplement neurologic examination with x rays, electrocardiogram, spinal fluid examinations and specialist consultation.
Psychogenic	In hysteria and malingering
Therapeutic	Induced by electricity and excessive doses of insulin or metrazol
Poisonings	Strychnine picrotoxin and caffeine poisoning Alcoholism and plumbism
Cardiovascular	With neurovascular disturbances such as hemorrhage thrombosis and edema With angiospasms and urticaria particularly in the allergies (p 547) Complete heart block hypertensive toxemia of pregnancy and malignant hypertension. Erythroblastosis fetalis

vestigation is inaugurated in order to prevent further recurrence The immediate program may be tabulated as undernoted

1 —*If respiration is embarrassed* start artificial respiration and send for pulmotor

of the month give *dilantin* in doses of 0 1 gm (1½ grains) three times daily continuing the phenobarbital for the first few dilantin days

Abortive Treatment—Abortive treatment is rarely possible since there is but a brief interval between aura and convulsion The potentially useful measures of therapy include inhalations of *100 per cent oxygen* the ingestion of *sugar* intravenous injection of *sodium phenobarbital* the rectal administration of a suspension of starch paste containing 1 to 2 drams of *paraldehyde* the use of an enema or a saline purge inhalations of *amyl nitrite* and relaxation in a warm bath

Treatment of the Convulsion—The physician rarely sees a convulsion the attack of petit mal or the psychic equivalents His main task in the presence of any of these is to prevent trauma Most epileptics are badly damaged as the result of overzealous therapy Teeth are loosened or knocked out by clumsy attempts to introduce a mouth gag and the throat is often traumatized during the same procedure

The patient is assisted gently to a recumbent position and protected from bruises during the course of the convulsion A gag is introduced if possible and bystanders are assured that recovery is imminent if only nature can be given an opportunity

Status Epilepticus—The treatment of status epilepticus requires heroic measures Intravenous injections of sodium phenobarbital or pentobarbital are given Lumbar puncture is performed to reduce increased intracranial pressure An enema is given and inhalations of oxygen containing 5 to 10 per cent carbon dioxide are advised

Surgery—The surgery of epilepsy holds considerable promise in isolated instances If there are any localizing phenomena an *exploratory craniotomy* is performed and attempts are made to relieve the effects of presenting pathology such as pressure from a cranial exostosis the presence of meningeal adhesions or a neoplasm

Institutionalization—Epileptics with mental or moral deterioration frequent attacks and episodes of status epilepticus are best institutionalized particularly if the members of the family are unable to care for the sufferer In well conducted farms or colonies the epileptic receives the benefit of well regulated hygiene and is removed from the tensions of the large world in which he is distinctly handicapped

Epilepsy and Marriage—The offspring of the epileptic has increased hazard of inheriting the parental affliction Marriage is associated with a real risk of transmission with which both contracting parties should be thoroughly acquainted before the marriage is consummated In the majority of the instances the advice of the physician is not sought until the wedding has taken place Under these circumstances it seems advisable to urge the use of *contraceptive measures* (p 2502) unless there are formidable religious objections

THE GENERAL MANAGEMENT OF CONVULSIONS

The convulsive state is marked by involuntary contractions of skeletal muscle These may vary from barely perceptible localized twitches to massive disturbances involving all of the muscle mass Convulsions that

SECTION XI

THE EYE

Associate Editor FREDERICK H THEODORE M D

2—*If tongue is caught between teeth* insert a metal gag to prevent further injury

3—*Avoid hypodermic injection of drugs* until the cause of the condition can be ascertained If necessary administer rapidly acting barbiturates (sodium pentothal) as in generalized intravenous anesthesia (p 3923) Avoid opiates and alleged circulatory stimulants

4—*Obtain history of previous attacks* (epilepsy) or the *use of drugs* or hypodermic substances administered with therapeutic purpose or for criminal or suicidal intent

5—*Obtain urine*, by catheter if necessary, and *test* for albumin and sugar If glycosuric and acidotic administer insulin and dextrose intravenously

6—With hyperpyrexia or insolation give *sponge baths* to reduce fever (p 3785)

7—*In suspected poisoning* perform gastric lavage and later a colon irrigation

8—With *excessive hypertension* consider phlebotomy

9—With history of *trauma* get skull x rays and summon neurosurgeon

10—With *bloody spinal fluid* adopt principle of 'skillful neglect' unless there is a clear history of trauma

11—With *turbid spinal fluid* and *suspected infection* inaugurate antibiotic therapy with intravenous penicillin

12—With suspected *cerebral edema* give intravenous injection of 50 per cent sucrose or dextrose (p 3824)

13—In *Jacksonian convulsions* remove patient to hospital for complete neurologic survey and exploratory craniotomy if necessary

14—In the *interval between attacks* get x rays of skull, complete neurologic and psychiatric status examinations tests of spinal fluid electroencephalograms and fundus examinations

15—If *status epilepticus* is present try warm baths or complete chloroform anesthesia

CHAPTER 75

INTRODUCTION PHYSIOLOGY METHODS OF EXAMINATION AND TREATMENT

The practitioner is concerned with clinical ophthalmology for its importance in problems relative to the visual apparatus and its *diagnostic significance* in the recognition of extra ocular phenomena The sclera shows earliest evidences of jaundice pupillary abnormalities are among the most reliable manifestations of cerebrospinal syphilis the optic nerve reflects the changes of many widespread disturbances of the central nervous system and the retinal arteries and veins which alone of the vascular struc

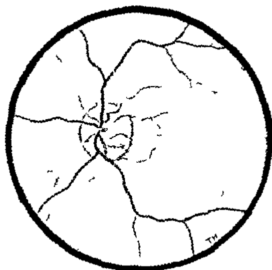


Fig 281 —Normal fundus with physiologic cupping

tures can be visualized often exhibit the herald signs of circulatory and renal disturbances at a time when prophylactic therapy is of immeasurable value

While it is not intended that the practitioner usurp the functions of the trained ophthalmologist (p 1540) he deprives himself and his patient of a vast fund of information unless he includes in his routine physical examination a careful survey of the eye particularly the information so readily available by the use of the *ophthalmoscope* (p 1545)

REVIEW OF ANATOMY

See p 3612

Gifford Textbook of Ophthalmology

Lpon entering the eye arterial pressure approximates 75 per cent [illegible] venous pressure is slightly in excess of intra-ocular pressure Maintenance [illegible]

DIFFERENTIAL DIAGNOSIS OF

Tearing (Epiphora)

The phenomenon of tearing may be due to excessive secretion or mechanical [illegible] with lacrimal drainage The latter is always of local origin but profuse lacrimation [illegible] result from distant causation.

	DIAGNOSTIC FEATURES
Psychogenic	Emotional disturbances
Visual	Eye strain and asthenopia Order re[illegible]act[illegible] (p 153[illegible])
Lacrimal	Stenosis of nasolacrimal duct E[illegible]ersion o[illegible] occlusion of lacrimal punctum Acute and chronic dacryocystitis Test patency by irrigation or probe (p 1557)
Adnexal	Ectropion, blepharochalasis (senile bagginess) or blepharitis Exophthalmos with lagophthalmos Note B.M.R.
Conjunctival	Foreign body photo retinitis burns and chemical irritants or conjunctivitis Examine by oblique illumination (p 3622) Make smears and cultures of exudate and epithelial scrapings (p 1546)
Corneal and Scleral	Episcleritis scleritis and keratitis Refer to specialist for slit lamp examination and epithelial scrapings
Uveal	Iridocyclitis with circumcorneal injection Refer to specialist for slit lamp examination Sympathetic ophthalmia following injury to sensitizing eye Urgent consultation with ophthalmologist
Disturbances of Intra-ocular Tension	Glaucoma with severe pain and increased tension Refer to specialist after instillation of miotic for symptomatic relief (p 1548) Avoid examination with mydriatics (p 1548)
Neurogenic	With facial paralysis including Bell s palsy
Systemic Infections	Rhinitis with upper respiratory symptoms Measles with cutaneous rash Pertussis with paroxysmal cough and lymphocytosis Influenza with respiratory manifestations and myalgias Mikulicz s disease with simultaneous swelling of submaxillaries
Allergy	Vasomotor rhinitis with nasal discharge containing eosinophils Vernal conjunctivitis with eosinophils in local spread
Metabolic Disturbances and Poisonings	Hyperthyroidism with elevation of B M P and therapeutic response to iodine Senility alcoholism, exposure to tear-gas and paraphenylendiamine poisoning

[illegible]ps is of importance in the circulation of *intra-ocular fluid* and the pathogenesis of *glaucoma* (p 1578)

PHYSIOLOGY

The essential visual function of the ocular structures is dependent upon protective vascular motor and sensory components

PROTECTIVE MECHANISMS

Besides the protection of the bony orbit the eye is defended by fibrous coats movements of the lids lubricatory secretions and the sensitivity of the cornea

Lid Movements—*Voluntary and involuntary movements of the lids are encountered Involuntary blinking occurs every two to ten seconds to moisten the cornea and sweep it clean Blinking helps drainage of tears and encourages the circulation of intra-ocular fluid* See *Blepharospasm (p 1619)*

Sensitivity of the Cornea—*Sensitivity of the cornea results in reflex blinking and an increased flow of tears at the slightest irritation Sensory fibers of the cornea are derived from the first division of the trigeminus*

Tearing (Epiphora)—Lubrication of the eye is accomplished by tears from the lacrimal gland and secretions from mucous glands Tears are slightly salty and alkaline their bacterial activity is due to the presence of a *lysozyme* After cleansing the eyeball tears pass down the lacrimal passages to the nose The nervous mechanism that is involved in lacrima

TABLE 101—*DIFFERENTIATION OF CONJUNCTIVAL AND CILIARY INJECTION OF THE EYE*

	Conjunctival Injection	Ciliary Injection
Involved Vessels	Posterior conjunctival	Posterior ciliary
Color	Brick red	Lilac
Location	Most marked in fornix with fading toward cornea	Circumcorneal with fading toward fornix
Appearance	Network *of coarse anastomosing vessels Altered by pressure on* lower lid	*Small straight vessels radiating from cornea* Unaffected by pressure on the lower lid
Discharge	Mucopurulent or purulent	Tears
Involved Tissue	Conjunctiva	*Cornea iris or ciliary* body

tion *has not been clearly worked out but it is interesting to note that psychic weeping occurs only in man*

THE CIRCULATION

The conjunctiva is supplied with blood vessels from posterior conjunctival and anterior ciliary arteries and veins The iris is nourished by long posterior ciliary branches of the ophthalmic artery and these with the central artery of the retina constitute the circulatory mechanism of the organs of vision The vessels of the eye are influenced by nervous and chemical controls Vasoconstrictor fibers are present but vasodilator structures have not been identified The presence of axone *reflexes* has been proved by the elimination of *painful* phenomena *after retrobulbar anesthetization*

The distinction *between conjunctival* and ciliary *injection* assists in the *differential diagnosis of ocular disease* See Table 101

Transparency of the *refractory media* (cornea aqueous lens vitreous and anterior layers *of retina*) requires a state of avascularity hence the nutrition of these structures is maintained by a process of diffusion The refracting media are highly susceptible to metabolic disturbances are infrequently attacked in systemic infection and possess little resistance once invasion has occurred The *uveal tract* (p 1619) *by contrast is the vascular portion of* the eye it suffers from few metabolic *diseases but infection occurs with greater frequency* and at immense threat to visual *functions*

Upon entering the eye arterial pressure approximates 75 per cent of brachial readings enous pressure is slightly in excess of intra-ocular pressure Maintenance of these relation

DIFFERENTIAL DIAGNOSIS OF

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The phenomenon of tearing may be due to excessive secretion or mechanical interference with lacrimal drainage The latter is always of local origin but profuse lacrimation also may result from distant causation

	DIAGNOSTIC FEATURES
Psychogenic	Emotional disturbances
Visual	Eye strain and asthenopia Order refraction (p 1530)
Lacrimal	Stenosis of nasolacrimal duct Eversion or occlusion of lacrimal punctum Acute and chronic dacryocystitis Test patency by irrigation or probe (p 1557)
Adnexal	*Ectropion blepharochalasis (senile bagginess)* or blepharitis Exophthalmos with lagophthalmos Note B M R
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Corneal and Scleral	Episcleritis scleritis and keratitis Refer to specialist for slit lamp examination and epithelial scrapings
Uveal	Iridocyclitis with circumcorneal injection Refer to specialist for slit lamp examination Sympathetic ophthalmia following injury to sensitizing eye Urgent consultation with ophthalmologist
Disturbances of Intra-ocular Tension	Glaucoma with severe pain and increased tension Refer to specialist after instillation of miotic for symptomatic relief (p 1548) Avoid examination with mydriatics (p 1548)
Neurogenic	With facial paralysis including Bell's palsy
Systemic Infections	Rhinitis with *upper respiratory symptoms* Measles with cutaneous rash Pertussis with paroxysmal cough and lymphocytosis Influenza with respiratory manifestations and myalgias Mikulicz's disease with simultaneous swelling of submaxillaries
Allergy	*Vasomotor rhinitis* with *nasal discharge* containing eosinophils Vernal conjunctivitis with eosinophils in local spread
Metabolic Disturbances and Poisonings	Hyperthyroidism with *elevation of* B M.R. and therapeutic response to iodine Senility alcoholism, exposure to tear-gas and paraphenylendiamine poisoning

...his is of importance in the circulation of *intra-ocular fluid* and the pathogenesis of *glaucoma* (p 1578)

INTRA OCULAR FLUID

Intra ocular fluid is of complex chemical composition and contains elements present in blood serum It appears to be a *dialysate* of capillary blood but may be a secretion of ciliary epithelium

Circulation of Intra Ocular Fluid —The circulation of intra-ocular fluid does not follow a definite pathway A constant renewal probably occurs through the vascularized tissues of the eye As a result of external pressure and thermal stimuli there is an intermittent flow from ciliary bodies through pupils into anterior chambers and out through the canals of Schlemm

Intra Ocular Pressure —Normal intra-ocular pressure (p 15"8) measures between 12 and 30 mm of mercury Tension varies 1 to 2 mm with the pulse beat, and rises 3 mm on inspiration It is highest in the early morning drops sharply on arising and increases again at night to reach its maximum The normal diurnal variation is 2 to 3 mm of mercury but in abnormal conditions such as *glaucoma* the swings are wider

Intra-ocular pressure is maintained by the elasticity of the outer coat of the eye and the volume of intra ocular fluid A safety valve action of the canal of Schlemm maintains relatively constant conditions

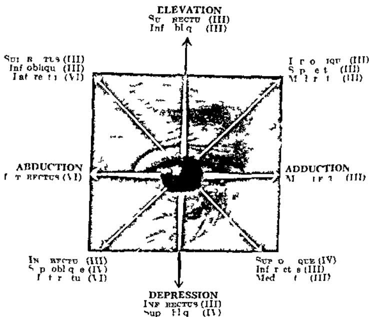


Fig 285 —Scheme of movements of the cornea of the right eye from the resting position with the muscles that affect them The predominant muscles are in capital letters the roman numerals after the names indicate the nerve supply (Adapted from Testut 1914)

Variations in Intra Ocular Pressure —Intra ocular pressure is subject to variations due to physiological and pathological conditions *Pressure on the globe* and the actions of extra ocular muscles raise the tension 4 to 10 mm of mercury Alterations in *arterial blood pressure* rarely causes corresponding changes in intra-ocular pressure but *venous pressure* changes are delicately reflected Occlusion of the retinal vein for example causes late glaucoma

Pressure of intra-ocular fluid is influenced by alterations in the volume of the contents of the eye With a general increase in the osmotic pressure of blood the eye loses fluid and tension drops This principle is utilized in the treatment of acute glaucoma (p 15"8)

OCULAR MOTILITY

The eye is rotated around three axes by extra-ocular muscles Each eye movement involves contraction of active muscles and inhibition of antagonists Rotation about the *vertical axis* is an *adduction* when the eye is turned toward the nose and an *abducti*[illegible] when the eye moves toward the temple Around the transverse axis the eye is e

Torsion movements about the *anteroposterior axis* are less obvious when the upper end of the vertical meridian is tilted toward the nose it is an *intorsion* and when it is tilted toward the *temple or outward it is an extorsion*.

The Cardinal Directions of Gaze.—The field of muscle action is that direction in which *its main action is greatest. Ocular movements are examined in six cardinal directions of gaze* Obvious pareses and overactions become grossly apparent, but the detection of slight involvement which is sufficient to *cause diplopia* (p. 1523) *requires screen testing* by the expert.

Conjugate Movements.—Regulation of ocular movements to achieve simultaneous action *is accomplished in* part by *various of the cerebral association centers* In associated or

TABLE 102.—OCULAR FUNCTIONS OF EXTRA-OCULAR MUSCLES

Muscle	Main Action	Subsidiary Action
Superior Rectus	Elevation Action increases as eye is turned out, becomes nil when eye is turned in	Adducts eye and rotates vertical meridian inward *(intorsion)* Action increases as eye is turned in
Inferior Oblique	Elevation Action increases as eye is turned in becomes nil when eye is turned out.	Abducts eye and rotates vertical meridian outward (extorsion) Action increases as eye is turned out
Inferior Rectus	Depression Action increases as eye is turned out, becomes nil as eye is turned in	Adduction and extorsion Action increases as eye is turned in
Superior Oblique	Depression Action increases as eye is turned in becomes nil as eye is turned out.	Abduction and intorsion Action increases as eye is turned out
Medial Rectus	Medial rotation	None
Lateral Rectus	Lateral rotation	None

TABLE 103.—PREDOMINANT MUSCLE ACTIONS INVOLVED IN EYE MOVEMENTS

Eyes Directed To	Muscles Predominantly Acting
Right	R lateral rectus L medial rectus
Left	R medial rectus L lateral rectus
Up and right	R *superior rectus* L *inferior oblique*
Up and left	R inferior oblique L superior rectus
Down and right	R inferior rectus L superior oblique
Down and left	R superior oblique L inferior rectus

conjugate movements the visual axes may be parallel or disjunctive in the latter type the visual axes may converge *(convergence)* or diverge *(divergence)* Loss of one or more conjugate movements may occur in disease despite normality of extra-ocular musculature

Binocular Vision.—The complicated mechanism of ocular motility is designed to insure *binocular fixation* by which the *image of an object falls* on the macula and corresponding points of the retina of each eye The two images are then fused into a single mental image in a theoretical cerebral *fusion center* This *faculty in its highest form*, permits stereoscopic or solid vision.

Failure of the image of an *object* to fall on *corresponding points of* the two retinas due

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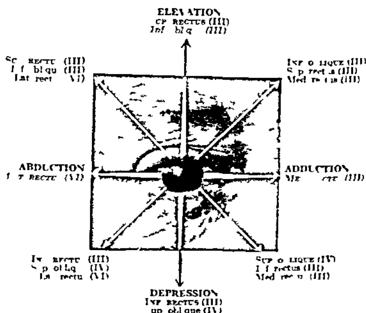


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Diplopia tests performed by the specialist to determine the muscle or muscles involved are accomplished by placing a red lens in front of one eye while moving a small light (ophthalmoscope bulb) in the six cardinal directions of gaze The examiner questions the patient concerning the amount of separation of red and untinted images Separation is greatest in the field of action of the involved muscle (Table 104) The true image corresponding to the fixing eye is distinct as it falls on the macula the "false" image of the deviating eye is less distinct.

Suppression —Suppression is a mental process by which the image of the deviating eye is not allowed to enter consciousness By this means unpleasant symptoms associated with *double images are automatically eliminated In concomitant strabismus (p 1529) a defective* fusion faculty is at fault and suppression is accomplished at the onset of the squint In paralytic strabismus of long standing the image of one eye usually the paralyzed eye may be entirely suppressed

OCULAR DEVIATIONS (PARALYTIC AND NONPARALYTIC STRABISMUS)

Ocular deviations may be paralytic (noncomitant) or nonparalytic (concomitant)

Paralytic Strabismus —The important characteristics of paralytic strabismus of the ocular muscles are (1) limitation of eye movement in the field of action of the paralyzed muscle,





A B

Fig 296—Right oculomotor paralysis *A* Primary position left eye fixing *B* Eyes *left*, right eye is held in abduction by contracture of external rectus

(2) increasing deviation of the affected eye as the eyes are turned into the field of action of the involved muscle (3) diplopia which becomes more marked in the field of action of the paralyzed muscle and (4) associated symptoms of nausea and vertigo

Nonparalytic Strabismus —Nonparalytic or concomitant strabismus (*heterotropia*) is the common type of *cross eye* encountered in childhood In contradistinction to the characteristics of paralytic strabismus *(1) the deviation from parallelism does not vary but is always* the same in amount in every direction of gaze (2) the power of the individual muscles is normal, as is demonstrable by covering one eye and having the patient rotate the other eye in all directions *(3) due to suppression neither diplopia nor other subjective symptoms are* encountered (4) the two eyes do not work as a pair the one sighting the envisioned object being the *fixing eye* while the other is the *squinting eye*

Squint.—Squint arises *from a disturbance of the delicate* balance between the *powers of* convergence and divergence in individuals with a congenital defect of the fusion faculty or the innate desire for binocular single vision In *monocular* squint the one eye constantly deviates and the other fixes vision in the *deviating eye* is generally poor In *alternating* squint the patient fixes with either eye and vision in each is good

Concomitant Strabismus (Heterotropia) —According to the direction of deviation *concomitant squints are convergent* (internal strabismus or esotropia) *divergent* (external

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to deviation of one eye results in *diplopia (double vision)* (p 1598) Due to the process of *projection* by which images striking the *upper* portion of the retina (for example) are in

DIFFERENTIAL DIAGNOSIS OF

Double Vision (Diplopia)

In double vision there is the recording of a true and a false image The latter may be situated laterally above or below the observed object

	DIAGNOSTIC FEATURES
Paralytic Strabismus	Of third, fourth or sixth cranial nerves Limitation of eye movement only in field of action of paralyzed muscles (p 1527) Complete neurologic examination and check cerebrospinal fluid (p 3734)
Nonparalytic Strabismus	Heterotropia of childhood Power of individual muscles is normal Screen test (p 1543)
Errors of Refraction and Accommodation	Asthenopia (eyestrain) Order refraction (p 1537)
Ophthalmic	Dislocation of lens Orbital cellulitis or tumors Symblepharon Exophthalmos Supplement local inspection with reference to specialist and estimation of B M R
Otogenic	Mastoiditis petrositis and labyrinthitis Examine ear-drums (p 2142) Get x rays of mastoid region (p 2146) Refer to otologist.
Neurogenic	Neoplasm inflammation, trauma or vascular injury to cerebrum or cerebellum Get neurologic status and examine fundi (p 3629) Suppurative and non suppurative encephalitides and meningitides Examine cerebrospinal fluid and get blood for virus neutralizing bodies (p 59) Tabes dorsalis and general paresis with positive serology and characteristic gold curves of cerebrospinal fluid Multiple sclerosis with pallor of optic disk, tremor and disseminated neurologic manifestations
Myogenic	Myasthenia gravis with therapeutic response to neostigmine (p 2886)
Psychogenic and Functional	Neuroses and hysteria Fatigue Ophthalmoplegic migraine
Metabolic	Diabetes mellitus with glycosuria and hyperglycemia Hyperthyroidism with elevation of B M R. and therapeutic response to iodine (p 611) Vitamin deficiency with therapeutic response to thiamine and niacin (p 616)
Poisonings	Alcoholism Addiction to cocaine Over-dosage with barbiturate Exposure to paraphenylenediamine
Systemic Infection	Diphtheria with ulceromembranous exudate containing organisms Botulism with history of ingestion of contaminated canned food

terpreted as coming from the *lower half* of the visual field diplopia is opposite in character to ocular deviation

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Fig 286—Right oculom otor paralys s A Pr mary position left eye fixing B Eyes left right eye is held n abduction by contracture of external rectus

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adrenergic or sympathetic fibers (p 1390) from the antagonistic subdivision of the involuntary nervous system

The pupilloconstrictor center is probably located in the accessory third nerve nucleus of Edinger Westphal Efferent fibers follow the third cranial nerve to the ciliary ganglion from which they pass to the eye by way of short ciliary nerves The pupillodilator center is the ciliospinal area of Budge Between pupilloconstrictor and pupillodilator centers there is a partial decussation and preganglionic fibers travel through the cervical sympathetic to the superior cervical ganglion whence post ganglionic fibers enter the skull with the carotid plexus, travel over the gasserian ganglion and accompany the ophthalmic division of the fifth cranial nerve to join the long ciliary nerves as they enter the eyeball In this way they avoid the ciliary ganglion

Innervation of Intra Ocular Muscles—The *dilator* muscle of the iris is innervated solely by adrenergic fibers Instillation of sympathomimetic amines such as epinephrine produces active contraction of the muscle and resultant mydriasis Paralysis of the nerve mechanism through destruction of the superior cervical ganglion (Horner's syndrome) results in miosis with narrowing of the palpebral fissure and enophthalmos

TABLE 104—THE VARIETIES OF STRABISMUS

	Paralytic Strabismus	Heterotropia	Heterophoria
Limitation of eye movement	In field of action of paralyzed muscle	None	None
Effect of turning eye into field of action of involved muscle	Increased deviation	*No increase in deviation from parallelism*	*No increase in deviation from parallelism*
Diplopia	More marked in field of action of involved muscle	None	Equal in all fields
Associated symptoms	Nausea Vertigo	None	Nausea, Vertigo
Screen test	When squinting eye is covered and uncovered no movement occurs in either eye When fixing eye is covered and uncovered both eyes move	When squinting eye is covered and uncovered no movement occurs in either eye When fixing eye is covered and uncovered both eyes move	Either eye when covered deviates but tends to swing back into place on uncovering

The *sphincter* muscle has double innervation being provided with stimulatory cholinergic nerves and inhibitory adrenergic nerves Depression or paralysis of the cholinergic mechanism by atropine and drugs of similar action produces mydriasis while stimulants such as physostigmine result in miosis

Pharmacology of Pupillary Reactions—Cholinergic nerve endings act through the liberation of acetylcholine which initiates the action of the innervated structure Acetylcholine is rapidly destroyed in the body by a choline esterase which is present in all tissues Pharmacologically the *effect of acetylcholine may be simulated by the instillation of available* derivatives such as acetyl beta methylcholine (mecholyl) and carbaminoylcholine (doryl) The latter exerts more powerful miotic effect since it is inactivated by tissue esterase only after several hours

Rapid destruction of choline compounds is inhibited by drugs with a carbamate group such as physostigmine (eserine) and neostigmine (p 1334) These combine and inactivate choline esterase and cause paralysis of the dilator mechanism with the production of miosis Pilocarpine and muscarin produce a similar effect but their mechanism of action is dissimilar since they are not destroyed by choline esterase

[illegible]gic nerve endings are stimulated by liberation of an epinephrine-like substance

strabismus or exotropia) or *vertical* (hypertropia) *Accommodative strabismus* exists when an uncorrected error of refraction causes excessive accommodation and excessive convergence *Non-accommodative strabismus* usually arises as a result of lack of use of an eye due to *anisometropia* (p 1536) which is a marked refractive difference between the two eyes or to impaired vision in an eye due to disease In the latter instance the blind eye generally turns out (exotropia)

Latent Strabismus (Heterophoria).—Latent strabismus (heterophoria) is the condition in which the eyes have a tendency to deviate but, due to a well functioning fusion faculty maintain binocular single vision with effort As the deviation is latent and not apparent, it must be demonstrated by the screen test in which fusion is broken According to the deviating tendency phorias are classified as *esophoria exophoria hyperphoria* and *hypophoria* A tendency of the vertical meridian to deviate from the vertical position is *cyclophoria*

Clinical Manifestations of Strabismus —Heterotropia gives no symptoms other than those resulting from the cosmetic appearance heterophorias may produce asthenopia headache blurring of vision diplopia, nausea and vertigo

Treatment of Strabismus —Concomitant strabismus (heterotropia) is treated by the specialist by the use of glasses orthoptic training and surgery or a combination of all three In accommodative squint the use of proper glasses may diminish the strabismus considerably or even cure it Orthoptic training or exercises of considerable value in some cases are



Fig 287 —*A* Concomitant convergent strabismus *B* Result of recession and advancement

attempts to establish the simultaneous use of both eyes It is often necessary to resort to *occlusion of the good eye by a patch or to diminution of the function of the good eye* by the prolonged use of atropine in order to stimulate vision in the squinting or amblyopic eye This necessary preliminary to orthoptic training should not be attempted if the vision of the eye cannot be improved to 20/70 The best results of orthoptic training are obtained in children between the ages of three to six years with exotropia or the phorias especially convergence insufficiency

After a trial of non-operative procedures for at least a year operation is indicated Surgery may be performed at any age and early operation has definite psychological advantages for the pre-school child Postoperative orthoptic training often is much more valuable than preoperative efforts

The treatment of *heterophoria* consists of correction of any associated refractive error by means of glasses the incorporation of prisms in hyperphoria and of orthoptic training Surgery is utilized rarely as a last resort

INTRA OCULAR MUSCLES AND PUPILLARY REACTIONS

Beside voluntary extra-ocular muscles the eye possesses unstriated muscles which control pupillary reactions The *sphincter* of the pupil and its *ciliary muscle* are innervated by the vagal or cholinergic system (p 1333) through oculomotor nerves The *dilator* is supplied by

* Gifford, Textbook of Ophthalmology

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nerve endings are stimulated by liberation of an epinephrin like substance

This effect is produced pharmacologically by cocaine ephedrine neosynephrine benzedrine and paredrine

Physiology of the Pupil —The pupil acts as a diaphragm for the eye It regulates the amount of light that falls on the retina contracting when there is high intensity and dilating when the intensity of illumination is low In this manner it improves the effectiveness of the eye as an optical instrument

The normal diameter of the pupil is about 3.5 mm It is wider in those with myopia and in the female It is smaller in those with hyperopia and at the extremes of age A pupil which is smaller than 2 mm under normal illumination is abnormally *miotic* (p 1533) One that is larger than 5 mm under similar conditions is normally *mydriatic* (p 1533) Inequality in the size of the two pupils is an *anisocoria* (p 1534) which may be physiologic or pathologic

Pupillary Reflexes —The normal pupil responds to a variety of sensory stimuli many of which have important significance in clinical medicine

Direct and Indirect (Consensual) Light Reflexes —Exposure of the retina to bright light results in contraction of the pupil (*direct light reflex*) The degree of effect varies with the relative change of illumination the state of adaptation of the eye and the intensity of the light stimulus The pupil of the unstimulated eye under normal circumstances should contract simultaneously and to equal degree (*indirect or consensual light reflex*)

The Near Reflex (Accommodation) —Focus of the eye on a near object results in accommodation convergence and pupilloconstriction The miosis occurs normally when accommodation and convergence are eliminated respectively by lenses and prisms The independence of light and accommodation reflexes is illustrated by the Argyll Robertson pupil (p 1534)

The Orbicularis or Lid Reflex —With the eye closed the pupil of the shut eye contracts as a reflection of a central mechanism

The Oculosensory or Trigeminal Reflex —The application of sensory stimuli other than light to the eye and its adnexa results in initial pupillodilatation followed by contraction The response is bilateral and is a true reflex mediated through the trigeminal nerve

Psychosensory Reflex —Stimulation of any sensory nerves except for those supplying the eye and its adnexa results in pupillary dilatation through a central response in the cortex

THE PHYSIOLOGY OF VISION

When light strikes the retina there occur chemical and electrical changes *Physical changes* include phototropic migration of retinal pigment toward the light contraction of the cones and swelling of the rods *Chemically* retinal tissue becomes acid and visual purple or rhodopsin is bleached a change in which *vitamin A* participates (p 617) The chemical reaction is reversible and is associated with measurable *electrical potential*

Scotopic and Photopic Vision (Duplicity Theory) —According to the duplicity theory two types of visual activity exist in the retina By means of the rods low intensities of light are perceived the scotopic type of vision is achromatic and is concerned with the appreciation of light and movement it is especially evidenced in conditions of dark adaptation Higher intensities of light are registered by the cones (*photopic vision*) which concern themselves with form and color vision Photopic vision is particularly evident in the light adapted eye with its relatively high threshold stimulus intensity

The Visual Sensations —Stimulation of the retina results in three types of visual sensation related to light, color and form

Light —Light sense is the faculty by which the eye distinguishes between light and dark and between differences in the brightness of illuminated objects This faculty is more sensitive than color or form senses and operates when illumination is sufficiently diminished to eliminate other types of sensations In the dark adapted eye an extremely slight degree of brightness evokes a sensation of light Disturbances of light sense (p 1535) consist of *night blindness* and *day blindness*

Color —Appreciation of color is a function of the cones or of the photopic mechanism of vision In good illumination the upper end of the spectrum appears brighter especially yellow In poor illumination the lower end of the spectrum especially blue is most easily visible (Purkinje's phenomenon) The *Young Helmholtz theory* of color vision postulates that all hues can be compounded from a mixture of the three primary spectral colors of red, green and violet. Normal color vision according to this theory is *trichromatic* and the retina contains three types of cones capable of producing sensations of red green and violet. Anomalies of color sense (p 1535) consist of *color blindness* and *perversions of col*

DIFFERENTIAL DIAGNOSIS OF

Abnormalities of Pupillary Diameter

The pupils may be excessively dilated (mydriasis) or contracted (miosis) Differences in pupillary size constitute anisocoria which is indicative of the unilateral operation of any of the provocative factors which cause bilateral mydriasis or miosis

	MYDRIASIS	MIOSIS
Congenital	Neuromuscular with normal vision Amaurotic with optic nerve atrophy *as in amaurotic family idiocy*	Neuromuscular with normal vision
Refractive	Myopia (p 1536)	Hyperopia (p 1536)
Oculomotor	Paralyses with associated ophthalmoplegia (p 1537)	Stimulation usually reflex and spastic
Disturbances of Superior Cervical Sympathetic	Irritation due to hyperthyroidism upper lobe pneumonia or unilateral pleurisy Get B M R in afebrile and chest film in the presence of fever	Paralysis from pressure of aortic aneurysm, mediastinal neoplasm or lymphadenopathy Get chest film Injury or surgical destruction of ganglion causing Horner s syndrome with enophthalmos and narrowing of palpebral fissure
Ophthalmic	Glaucoma with increased intraocular tension Keratitis with observable lesion Amaurosis due to optic nerve atrophy degenerative retinitis or occlusion of retinal arteries Note ophthalmoscopic findings (p 3628)	Keratitis and iritis with circumcorneal injection (p 1524) Slit lamp examination (p 1544)
Neurogenic	Paralysis of pupilloconstrictor or stimulation of pupillodilator centers from cerebral tumor vascular accident or encephalitis Note other neurologic changes Tabes dorsalis general paresis and syphilitis meningitis with positive serology and changes in cerebrospinal fluid. Suppurative and non suppurative encephalitides and meningitides with other neurologic findings and changes in cerebrospinal fluid. Multiple sclerosis syringomyelia and transverse myelitis with other motor and sensory findings	Stimulation of pupilloconstrictor or paralysis of pupillodilator mechanisms from same causes as produced mydriasis
Pharmacodynamic	Atropine and atropine like substances Sympathomimetic amines such as epinephrine and related substances Acute alcoholism and overdosage with general anesthetics hypnotics and sedatives	Physostigmine and allied substances Opiate and morphine poisoning

DIFFERENTIAL DIAGNOSIS OF

Pupillary Abnormalities Other Than Mydriasis and Miosis

Other than dilatation and contraction abnormalities of the pupil may have important diag nostic significance mo t particularly but not exclusively in cerebrospinal syphilis

	DIAGNOSTIC FEATURES
Irregular Pupils	Glaucoma with increased intraocular tension *Iritis and keratitis with changes observed in* slit lamp and circumcorneal injection (p 1534) General paresis tabes dorsalis and syphilitic meningitis with positive serology and characteristic changes of the gold curv (p 3736)
Argyll Robertson Pupil (Paralysis of Light Reflex with Retention of Near Reflex or Accommodation)	Glaucoma with increased intraocular tension General paresis tabes dorsalis and syphilitic meningitis Organic neurologic conditions, such as encephalitis meningitis poliomyelitis *multiple neuritis due to diabetes* mellitus or avitaminosis multiple sclerosis and syringomyelia Complete neurologic examination and tests of blood urine and spinal fluid
Inverse Argyll Robertson Pupil (Paralysis of Near Reflex with Retention of Light Reflex)	Cerebrospinal syphilis with positive findings in blood and spinal fluid Diphtheria with ulceromembranous inflammation Tumors of corpora quadrigemina with other neurolog c findings
Paralysis of Light and Near Reflex but Retention of Lid Reflex	Supranuclear lesions at the termination of afferent paths Refer to specialist consultant.
Loss of Psychosensory Reflex	Severe organic disturbances such as idiocy imbecility chronic alcoholism and general paresis Examine blood and spinal fluid
Hippus (Rhythmic Contractions and Dilatation of Pupils)	With paralysis of internal and external ocular muscles in hemiplegia multiple sclerosis and meningitis Get complete neurologic survey and check cerebrospinal fluid (p 3734)
Pupillary Nystagmus	With ocular nystagmus in epidemic enceph alitis and hypertensive toxemia of pregnancy
Cyclic Oculomotor Paralysis (With alternating Phases of Elevation of Upper Lid, Contraction of Pupil Convergence and Accommodation followed by Ptosis Mydriasis and Pupilloparalysis)	Congenital anomaly
Springing Pupil (Sudden momentary Pupillodilatation)	Cerebrospinal syphilis with positive findings in blood and spinal fluid (p 3736) Neurasthenia Veronal poisoning (p 3836)
Myotonic Pupillary Reaction (Sluggish Light Reflex with Continuation of Miosis after Removal of Stimulus)	With absent knee jerks in Ad e s syndrome a non syphilitic affliction Note normal blood and spinal fluid

Form—Form sense is concerned with the abil ty of the eye to perceive the shape of ob jects In practice form sense is measured by charts of *visual acuity* (Snellen) It is a photopic mechanism l pendent upon the retina cones *of which the human eye possesses* 200 000 to the square millimeter The unusually keen vision of the eagl is said to be du to its cone population at the fovea, of 1 000 000 cones to the square millim ter

THE EYE AS AN OPTICAL INSTRUMENT

In passing through the eyeball to be *converged on the retina rays of light are refra ted* by cornea and anterior and posterior surfaces of the crystalline lens

DIFFERENTIAL DIAGNOSIS OF

Disturbances of Color, Light and Form Sense

Disturbances of the color light and form senses are not often encountered, though they may be of important diagnostic significance

	DIAGNOSTIC FEATURES
Color Blindness (Achromatopsia)	Congenital anomaly Hysteria Malingering Optic atrophy or neuritis Examine fundus and test with pseudo-isochromatic charts (p 1541)
Perversions of Color Sense (Chromatopsia)	Green vision with digitalis Yellow vision with picric acid and santonin Erythropsia (red vision) following cataract extraction Xanthopsia (yellow vision) in jaundice
Day Blindness (Hemeralopia)	Albinism. Toxic amblyopia colobomas and irideremia Refer to specialist
Night Blindness (Nyctalopia)	Vitamin A deficiency with response to therapeutic tests Oguchi s disease in Japanese Simple glaucoma with elevation of intra-ocular tension Choroideremia and retinitis pigmentosa—refer to specialist Hysteria
Metamorphopsia (Changes in the Shape of Objects) Micropsia and Macropsia (Changes in the Size of Objects)	Exudative choroiditis with circumcorneal injection and ophthalmoscopic findings (p 1534) Retinitis and detachment of the retina with fundus changes Refer to specialist
Photopsia (Flashes of Light and Bright Circles)	Migraine and epilepsy with characteristic *history Exudative choroiditis and detachment* of retina with fundus changes

R f act on —Rays of light pass out in all directions from any lum nous po nt Rays which emanate from a source less than 20 feet distant diverge but rays travell ng in excess of 20 feet are assumed to be parallel

When the ray of light meets an opaque body it is *absorbed* or *reflected* A transparent body permits pas age of the greater part of the ray with some deflection Bending of the ray is described as *ef act on* The *ndex of ref action* is the comparative length of time that it takes light to t avel a defin t d stance in d fferent transparent med a If a r is taken *as unity the index of refraction of water is 1 33 of the cornea 1.33 of the l ns 1 40* and of crown glass of the type usually used in optical procedures 1.5

Acc *mmodat on*—The ability or power to increase the refract ve or focus ng power of the eye is *accommodat on* Th s is accomplished by an increase in convexity of the crystalline lens According to the Helmholtz theory the ci ary muscle contracts the choroid is drawn forward to r lax th suspensory l gament or zonul tens on on th l ns capsul is released

DIFFERENTIAL DIAGNOSIS OF

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Other than dilatation and contraction abnormalities of the pupil may have important diagnostic significance most particularly but not exclusively in cerebrospinal syphilis

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in front of the retina *Astigmatism* is a more complicated disturbance in which there is an abnormality of refraction which differs in the several meridians

DISTURBANCES OF ACCOMMODATION

The principal disturbance of accommodation is *presbyopia* in which advancing age results in a physiological weakness of the accommodation mechanism and the characteristic inability of the older individual to focus for near vision *Spasm of accommodation* occurs more frequently in younger patients and is in all likelihood a neuromuscular disturbance often of toxic origin In *anisometropia* there is inequality in refraction with consequent visual difficulty With *aniseikonia* the retinal images are unequal

ASTHENOPIA (EYESTRAIN)

Eyestrain may result in a variety of symptoms The purely visual complaints include blurring of vision lacrimation blinking blepharospasm spots before the eyes a sandy feeling in the eyes and redness of the conjunctiva The more distant complaints include headache vertigo and nausea

Treatment—Asthenopia requires both systemic and local therapy The patient with eyestrain should be given instructions as to correct illumination the avoidance of eyestrain and the means of preventing physical fatigue Weakness of accommodation may be ameliorated by eye exercises spasms are sometimes alleviated by discontinuance of smoking and the use of mild sedatives such as sodium phenobarbital 15 mg (¼ grain) with or without an antispasmodic such as pavatrine 2 mg (1/30th grain) Main reliance however in the ametropias and presbyopia is placed upon the correctly fitted eyeglass

Eyeglasses—The refractive properties of glass are employed in the prescription of corrective spectacles which contain prisms or lenses Hyperopia and presbyopia are compensated by convex spherical lenses while myopia is improved by concave spherical lenses An eyeglass prescription for astigmatism is considerably more complicated and is specialist province

Prisms—A prism is a piece of glass or other substance bounded by plane surfaces inclined toward each other The thin edge where the surfaces meet is the *apex* and the opposite thick portion is the *base* Rays of light passing through a prism are bent toward the base Since the eye sees things reversed an object seen through a prism *appears* displaced toward the apex Prisms are used (*1*) to counteract the effects of ocular deviations due to muscle pareses (*2*) to exercise weak muscles (*3*) to test muscular power (*4*) to measure and test for heterophoria and heterotropia (p 1531)

Lenses—A lens is a transparent refracting medium usually glass in which one or both surfaces are curved There may be spherical or cylindrical lenses *Spherical lenses* are segments of spheres which refract ray of light equally in all meridians or planes *Convex spherical* or *plus* (+) *lenses* are thick at the center and thin at their edges They may be considered as two prisms with bases joined together in the center they converge parallel rays to a focus *Concave spherical lenses* or *minus* (—) *lenses* are thin in the center and thick at the edges They may be considered a

and the elastic capsule moulds the softer cortex into a more spherical shape Associated with accommodation contraction of the pupils and convergence occur

When the normal or emmetropic eye is at rest parallel rays from a distant object are focused on the retina but rays coming from a near object are focused behind the retina and that object appears blurred By accommodating the eye its refractive power is increased enough to focus these rays on the retina and the near object becomes distinct The normal eye must accommodate +3 D to read at 33 cm Accommodation involves muscular work and nervous strain

Accommodation is measured by bringing fine print up to the eye of a person who wears his required distance correction The distance from the eye at which the object becomes *blurred is noted in centimeters One hundred is divided by this and the quotient is the accommodative power* in diopters

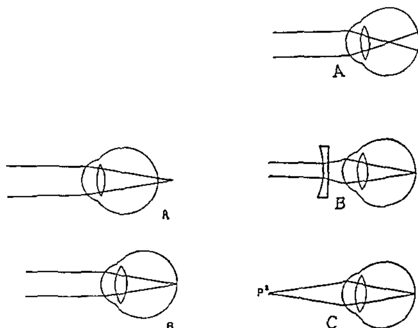


Fig 288—Hyperopia *A* With accommodation relaxed *B* Effect of accommodation on parallel rays *

Fig 289—Myopia *A* Parallel rays cross in front of retina *B* Effect of concave lens on parallel rays *C* Divergent rays from the punctum P² focus on retina without the use of accommodation *

ABNORMALITIES OF REFRACTION AND ACCOMMODATION

Errors in refraction or accommodation constitute the commonest causes for *asthenopia (eyestrain)* Either of these difficulties results in failure of the visual image to focus on the retina producing both visual and distant symptomatology which may be incapacitating to minor or major degree

ERRORS OF REFRACTION (AMETROPIA)

With normal refraction (emmetropia) the image is focused on the retina Abnormal refraction is productive of ametropia which may be of several varieties In far sightedness (*hyperopia*) the image is focused behind the retina whereas in near sightedness (*myopia*) the image is focused

* Gifford Textbook of Ophthalmology

vision of each eye Similarly the left optic tract consists of fibers from the left half of each retina or the right half of the field of vision of each eye

The optic tracts run laterally and backwards sweeping around the cerebral peduncles (crura cerebri) to end in two roots The lateral and larger root passes to the lateral geniculate body the pulvinar of the thalamus and the superior colliculus The smaller medial root goes to the medial geniculate body All the visual fibers are contained in the lateral root

The Lateral Geniculate Body—The lateral geniculate body receives the great majority of the visual fibers of the optic nerve which are relayed from it to the occipital cortex as the geniculo-calcarine pathway

The Superior Colliculus—The fibers that terminate in the superior colliculus are relayed to the nuclei of nerves III IV and VI They probably include pupillary fibers to the Edinger Westphal nucleus There are no efferent cortical fibers

The Pulvinar of the Thalamus—The pulvinar has apparently no part in the visual process in man but is concerned with ocular movements and stereognosis

The Visual Cortex—The geniculo-calcarine pathway makes its way through the temporal lobe and through the posterior portion of the internal capsule to form the optic radiations which end in the *area striata* of the occipital lobe surrounding the *calcarine fissure* The

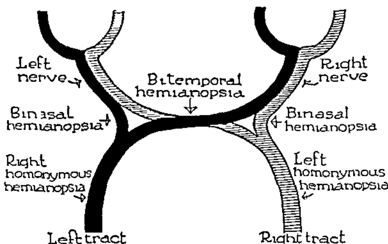


Fig 290—Hemianopsia

right visual cortex is concerned with visual impulses from the right half of each retina or the left field of vision

The Blood Supply to the Visual Pathways—The *chiasm* is supplied by branches from internal carotid anterior cerebral and anterior and posterior communicating arteries The *tract* is supplied by vessels derived from the posterior communicating and internal carotid arteries The *external geniculate body* is supplied by the posterior cerebral artery as is the main portion of the optic radiations The *visual cortex* receives its nourishment from the calcarine and other branches of the posterior cerebral artery

HISTORY

The patient with disturbances of the visual apparatus may complain of distant or local disturbances The more frequent remote complaints include headache (p 1512) and vertigo (p 2020) The more direct phenomena include the complaints of failing vision (p 1638) eyestrain (p 1537) conjunctival discharge (p 1619) excessive tearing (p 1525) photophobia (p 1574) and pain in the eye (p 1582)

A family history of similar difficulties suggests the presence of cataracts glaucoma myopia or the allergies A past or present history of

formed of two prisms whose apices are together in the center concave lenses diverge parallel rays of light

Cylindrical lenses or *cylinders* are segments of a cylinder parallel to its axis Light passing in the meridian or plane of the axis is not refracted and passes through unchanged as through a pane of glass Light passing through in a plane opposite or *perpendicular meets the curved surface* of the lens and is refracted The rays are converged or diverged depending on whether the cylinder is convex or concave It is necessary to indicate the axis or zero direction of a cylinder in an optical prescription

The Numeration of Lenses—The distance between the lens and the point at which it brings parallel rays to a focus is the *principal focal distance* The stronger the lens the shorter is this distance the strength of a lens is thus reciprocal to its focal distance The metric or dioptric system is used to classify lenses A lens whose principal focus is one meter distant is a 1 00 diopter (D) lens If it is stronger and has a focal distance of 0 5 or 0 2 meters it is a 2D or 5D lens respectively If it has a focal distance of 4 meters it is a 0 25D lens The spherical or cylindrical lens is a simple lens one that is both spherical and cylindrical is a *compound lens*

Contact Lenses—Contact lenses are thin shells of transparent glass or plastic material designed to be worn over the anterior portion of the eye ball They consist of a central portion which overlies but does not touch the cornea and a peripheral part which rests upon the sclera The space between the cornea and the contact lens is filtered with saline or isotonic buffer solution By its very nature corneal astigmatism is eliminated and *corrections for ametropia are ground into the glass*

The fitting of contact lenses is difficult The best and most improved method is to make a mold of the cornea and adjacent sclera under local anesthesia and to use this mold for casting the contact lenses

Contact lenses are of greatest value in keratoconus irregular astigmatism high myopias and for actors actresses and athletes The major objections to their use are the expense and the fact that the patient can tolerate them for only a number of hours

Protective Lenses—Tinted lenses are used for patients who *complain* of glare for workers exposed to bright reflected or fluorescent light and during exposure to strong sun or ice glare Sunglasses should be made of carefully polished lenses as inferior products contain irregular amounts of refractive strength and cause asthenopia

THE VISUAL PATHWAYS

The visual process begins in retinal rods and cones The light impulse is transmitted to *ganglion cells of the retina* whose axones continue in the nerve fiber layer converging to the *optic disk* Here they form the *optic nerve* which terminates intracranially at the *optic chiasm*

The Optic Chiasm—The optic chiasm is formed by the junction and partial decussation of the two optic nerves It is a transversely oval body 30 x 8 x 4 mm and usually lies behind the tuberculum sellae although its position may vary to some extent *It may be* above in front of or behind the *pituitary body* (p 1159) The inner fibers of the optic nerves decussate in the chiasm

The Optic Tracts—*Axones* emerge from each posterolateral aspect of the chiasm to form *the optic tracts* Each optic tract contains fibers from each eye The right is made up of non-decussating fibers from the right or temporal half of the retina of the right eye and decussating fibers from the right or nasal half of the retina of the left eye Thus the right optic tract contains fibers from the right half of each retina or the left half of the field of

Examination for Visual Acuity—Visual acuity is tested by the *chart* previously described (p 1535) If there is any abnormality the ophthalmologist performs *refraction* (p 1535) In a patient below the age of forty five a cycloplegic is employed if there is any question of the visual acuity The patient is tested with and without correction

Retinoscopy permits the ophthalmologist to estimate the refractive error by noting through the retinoscope the movement of a shadow like reflex in the eye This procedure which is particularly accurate when the eye is dilated with a cycloplegic and mydriatic is the best method of estimating the refraction in children or in those adults who are mentally deficient When the shadow like reflex has been observed the ophthalmologist tries lenses before the eyes and notes the reversal of direction when the proper lens is inserted Unlike refraction retinoscopy does not require the cooperation of the patient and is an objective procedure

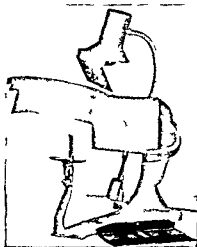


Fig 991 —Simplified Ferree-Rand perimeter *

Examination for Color Sense—The ophthalmologist uses the pseudo-isochromatic chart of Stilling or Ishihara to provide a rapid and accurate differentiation of the color blind These charts are invaluable in excluding malingerers

Examination for Light Sense—The adaptometer used for determining light sense is an expensive instrument that is not very accurate Few ophthalmologists use the machine since the light sense may be evaluated by questioning the patient concerning the length of time that it takes to find a seat in the movies when he passes from a light lobby into a darkened theater and the effect in night-driving of the headlights of oncoming automobiles

Examination for Visual Fields—In estimating and plotting the visual fields the ophthalmologist performs a preliminary confrontation test (p 3627) in the same manner as the practitioner For more detailed work a *perimeter* is employed This instrument is a metallic semicircle repre

* Clark in Pullen, Medical Diagnosis.

hypertension 'kidney trouble' diabetes tuberculosis or syphilis gives intimation that the ocular manifestation may be a local consequence of a systemic disturbance The previous use of quinine salicylate arsenicals reducing drugs (dinitrophenols) worm medicines' and laxatives containing phenolphthalein directs attention to possible drug idiosyncrasy or poisoning Ocular lesions which date to birth are most likely congenital anomalies or infections resulting from gonorrhea or neonatal syphilis At the extremes of life disturbances of the visual tract are most commonly due to presbyopia cataract or glaucoma

METHODS OF EXAMINATION

The practitioner is required to make a careful survey of the visual apparatus He inspects the eye by *oblique illumination* (p 3622), he tests visual acuity roughly with *reading charts* the color sense is approximated by *descriptions of objects in the room* dark adaptation becomes apparent from the *history* the visual fields are grossly marked out by the *confrontation test* (p 1541) In our opinion *ophthalmoscopy* (p 3628) is as much a part of the routine physical examination as auscultation and percussion

THE OPHTHALMOLOGIST

The positive indications for reference to the specialist ophthalmologist are

1 *Abnormalities* of the uveal tract (p 1632), the retina, media optic nerve or any of the visual functions (p 1638)
2 Investigation of *headache* (p 1512)
3 Investigation of *increased intracranial pressure* (p 1468)
4 Suspicion of the presence of a *brain tumor brain abscess* or trauma to the cranium such as a *fracture concussion laceration* of the brain or *intracranial bleeding*
5 *Meningeal irritation* (p 1462)
6 In *cardiovascular-renal disorders* (p 2379)
7 In *chronic disease* such as *tuberculosis* and *syphilis*
8 Exact determination of *visual acuity* (p 1541)
   (*a*) Charts
   (*b*) Refraction
   (*c*) Retinoscopy
9 Examination for *color sense* (p 1535)
10 Examination for *light adaptation* (adaptometer) (p 1535)
11 Examination of *visual fields* (p 1541)
   Perimetry stereocampimetry and angioscotometry
12 Examination for *ocular dominance* (p 1527)
13 Irrigation of *lacrimal passages* (p 1557)
14 Transillumination *of the orbit* (p 3632)
15 The use of the *slit lamp* (p 1544)
16 *Gonioscopy* (p 1545)
17 *Tonometry* (p 1545)
18 *Ophthalmoscopy* (p 3628)
19 *Exophthalmometry* (p 1546)
20 *Tests for squint* (p 1529)

screen is a large black cloth marked off with circles indicating the number of degrees of deflection from the central line of fixation of the eye The patient sits at a distance of 1 to 2 meters from the screen and focusses on its center A small dense object no more than 1 to 2 mm in size is employed and any defect (scotoma) in the central field is noted and measured A more elaborate device is the *campimeter* which is smaller and used at a lesser distance from the eye The *stereocampimeter* permits the patient to be examined with both eyes open at the same time The meas

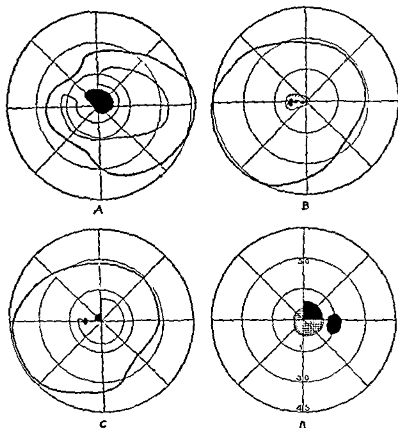


Fig 293—*A* Central scotoma retrobulbar neuritis *B* Paracentral scotoma with nuclei tobacco amblyopia *C* Uniocular quadrantic central scotoma junction scotoma *D* Chiasmal scotoma with quadrantic differentiation

urement of the size of the scotoma produced by the retinal vessels is termed *angioscotometry*

Tests for Ocular Dominance —In children who complain of reading difficulties the determination of the dominant eye is sometimes of value The ophthalmologist tests this by having the patient look into the wider end of a cardboard cone shaped like a megaphone The patient fixes upon an object in the distance Although apparently looking with both eyes due to the narrowness of the small end of the cone the object is fixed

Traquair in Berens The Eye and Its Diseases

senting 1 meridian of the hemisphere The apparatus can be revolved so that each meridian may be successfully studied The patient places the chin in a rest and focusses one eye upon a central focal point The other eye is closed The examiner then uses white and colored objects of known size to chart the exact limits of the visual field

The normal visual field is expressed in relative terms since it varies within limits depending upon the intensity and size of the stimulus employed Using a 3 mm white object on a perimeter of a 330 mm radius the peripheral limits of the field approximate 95 degrees outward 75 degrees downward 60 degrees inward and 60 degrees upward It is not uncommon to encounter a smaller field with a restriction of 10 degrees in

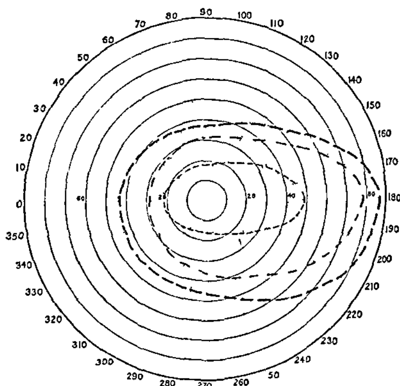


Fig 992 —Fields for 10/330 blue red and green Note the horizontal elongation of the color fields Average of six subjects *

all meridians The field for color is smaller than that for white but has the same general contour Red is 10 degrees less than blue and green 10 degrees less than red

Normally there is present *a physiological blind spot* which corresponds to the penetration of the retina by the optic nerve The center of the blind spot is about 12 to 15 degrees outside of the fixation point and 1½ degrees below the horizontal meridian It measures approximately 7½ degrees in height and *5½ degrees in width*

The central 30 degrees of the visual field are studied against a black background by means of a tangent screen or a campimeter The tangent

* Traquair in Berens The Eye and Its Diseases

("floaters") an aqueous ray or translucent beam is seen Early and subtle changes in the iris fine particles in the retro lental space and the localization of lenticular opacities in early *cataract* (p 1592) can be observed accurately with the slit lamp

Slit lamp study of the *vitreous* (p 1544) is sometimes unreliable but definite changes are noted in *hemorrhage* and long standing *inflammation*

Gonioscopy —The details of the angle of the anterior chamber are studied by using a special contact glass placed over the eye strong illumination and a magnifying device such as the slit lamp corneal microscope or an instrument known as the gonioscope These methods of ex



Fig 295 —Tonometer of Schiotz being placed on the cornea

amination are useful in glaucoma tumors of the iris and ciliary bodies and in localizing foreign bodies

Tonometry.—For a more accurate measurement of the intra ocular tension (p 1526) the ophthalmologist uses a tonometer which records the resistance offered by the anesthetized cornea to a definite weight It does not measure directly the intra ocular tension but is calibrated against an experimental setup in which actual intra ocular readings are recorded The limits of normal with the Schiotz instrument are considered to be between 15 and 29 mm of mercury In some people 29 is higher than the eyes can tolerate while others may tolerate far more without any ocular deterioration See *Glaucoma* (p 1578)

Ophthalmoscopy —The ophthalmologist uses the direct ophthalmoscope as does the practitioner While atlases are available with plates of the

Gifford Textbook of Ophthalmology

with only one eye The eye that does the looking is the dominant eye Most right handed individuals have a dominant right eye Many children *with reading difficulties have dominance of the left eye* usually associated with left handedness Retraining treatments consist of compelling the patient to use the right eye if necessary occluding or covering the left

Irrigation of the Lacrimal Passages—In order to determine patency of the lacrimal passages the ophthalmologist irrigates fluid by means of a blunt lacrimal needle into the canaliculus If the fluid flows unimpededly into the nose or throat there is no significant obstruction This procedure is painless in contradistinction to probing of the lacrimal passages

Transillumination—The ophthalmologist uses the ophthalmoscope light as a transilluminator The head of the apparatus is detached and the bulb is placed deep in the orbit through the lid or anesthetized conjunctiva The *pupil is observed for obstruction of light reflection by a tumor vitreous* hemorrhage or neoplasm Transillumination is also used to demonstrate *atrophy* of the *iris* In this condition fine points of light become evident in the iris during the procedure

The Slit Lamp—By means of the slit lamp the ophthalmologist obtains a magnified binocular view of the front half of the eye The slit lamp



Fig 294—Optic section through the eye produced by the narrow beam of light of the slit lamp *H* cornea *V* anterior chamber *L* lens *G* vitreous

consists of a binocular microscope magnifying objects twenty or forty times A special light projects a sharply defined focussed beam into the eye The beam traverses the part to be examined showing it in optical section while the remainder of the eye remains in darkness The lighting system is very flexible and the light can be so directed as to give direct focal illumination retroillumination or specular reflection The width of the beam may be widened or narrowed as desired The method permits the magnification of the area or tissue and localization of lesions according to depth

The slit lamp shows all types of *inflammation of the cornea* (p 1626) involving the epithelial layers and the deeper structures Vascularization an important indication of certain types of inflammation is apparent by retro illumination The appearance and size of the corneal nerves and the character of the endothelium of the cornea can be noted Finely pigmented or white precipitates may be seen on the posterior surface

In *iritis* (p 1633) when the aqueous contains fine floating particles

Alfred Vogt

A *mononuclear response* in the epithelial scrapings suggests epidemic virus keratoconjunctivitis or the milder Beal type of conjunctivitis in vernal conjunctivitis *eosinophilia* is demonstrable inclusion bodies are found in *trachoma* and *inclusion conjunctivitis* Giemsa stains are particularly valuable in the demonstration of pathogenic cocci

BIOPSY

Biopsy of the conjunctiva may reveal the presence of a *leptothrix infection* as in *Parinaud's conjunctivitis* It is also of value in the recognition of *tumors*

TREATMENT OF OCULAR DISORDERS

The practitioner can make considerable progress in the treatment of most ocular disorders by external applications methods of physical therapy and minor surgical procedures More serious ophthalmologic disorders are best referred to the specialist

LOCAL APPLICATIONS

Local applications are applied to the lids and eyes for purposes of cleansing (collyria) protection pupilloconstriction pupillodilatation local anesthesia bacteriostasis and bactericidal effects

DIFFERENTIAL DIAGNOSIS OF OCULAR DISORDERS

The differential diagnosis of ocular disorders has been tabulated in several places with reference to the presenting symptoms or signs The most important of these are *Epiphora (Tearing)* (p 1525) *Diplopia (Double Vision)* (p 1528), *Mydriasis and Miosis* (p 1533) *Abnormalities of the Pupils other than Mydriasis and Miosis* (p 1534) *Disturbances of Color Light and Form Sense* (p 1535) *Photophobia* (p 1574) *Exophthalmos (Proptosis)* (p 1575) *Papilledema (Choked Disks)* (p 1579) *Pain in the Eye* (p 1592) *Disturbances of the Eyelashes and Eyelids* (p 1612) *Disturbances of the Orbit* (p 1615) *Disturbances of the Conjunctiva* (p 1627) *Alterations in the Acuity of Vision (Amblyopia Amaurosis Dimness of Vision and Blindness)* (p 1638), *Ptosis (Lid Lag)* (p 1649) *Disturbances of the Fields of Vision (Hemianopia and Hemianopsia)* (p 1645) *Nystagmus* (p 1534)

PHYSICAL THERAPY FOR THE EYE

Physical therapy for the eye is accomplished by heat and cold infrared ray diathermy roentgen ray hyperthermia grenz rays phototherapy massage and iontophoresis

Heat and Cold—Heat causes active hyperemia absorption of products of inflammation and increase in local antibodies *Hot moist compresses* are best applied with pieces of cotton or cloth wrung out in water as hot as can be tolerated They are placed upon the closed lids and renewed every minute Running hot water from a washstand is as serviceable as boric acid Compresses are useful in inflammations of cornea ciliary body iris sclera and orbit They hasten the formation of pus and relieve pain in hordeola incipient chalazia lacrimal abscess and panophthalmitis Heat is contraindicated in conditions accompanied by intra ocular hemorrhage

Cold produces constriction of small vessels and lessens swelling which

commoner abnormalities the importance of positive findings is such that the specialist should be consulted for confirmation of the ophthalmoscopic picture and its interpretation A binocular view of the fundus is obtained by the *Gullstrand ophthalmoscope* a large expensive instrument not in general use

Exophthalmometry —Several methods are available to the specialist for the measurement of *proptosis* or *exophathalmos* (p 1575) The most common procedure is the use of the Hertel exophthalmometer This instrument is placed against the sides of the orbit and the protrusion of the eyeball is measured on a millimeter rule by a system of mirrors The intra orbital distance is noted for subsequent comparative examinations

The normal readings are between 16 and 18 mm at 96 to 100 intra orbital distance A proptosis of 20 is definitely pathological Increasing readings are of more value than a single observation See *Hyperthyroidism* (p 1197)

Recording Eye Movements —Using a special machine eye movements may be recorded This is of value in those who have reading difficulties and is often an initial step in the reeducation of patients with reading problems

LABORATORY EXAMINATIONS IN DISEASES OF THE EYE

Because the eye frequently reflects local manifestations of systemic disturbances (p 1598), it is essential to perform complete laboratory examinations in the presence of any ophthalmologic disorder These must include *serologic tests for syphilis hemogram urine analysis* and if indicated a *tuberculin test* and a *chest radiograph* With exophthalmos a *basal metabolic determination* is required With *papilledema roentgenologic examination of the skull lumbar puncture* and a review of the complete *neurologic status* become mandatory

BACTERIOLOGY OF THE EYE

Bacteriologic investigations of the eye often yield important information *Cultures* are made by briskly rubbing the conjunctiva of the lower lid with a sterile cotton applicator which has been moistened with glucose broth The material is immediately inoculated on a *blood agar plate* Using separate swabs the lid margin is treated similarly to culture hair follicles and glands Culture of a corneal ulcer is accomplished with a platinum loop After the agar plate has been inoculated secretion is smeared on a glass slide and stained by the Gram method for immediate examination Recognizable pathogens include staphylococci streptococci pneumococci meningococci gonococci H influenzae H conjunctivitidis (Koch Weeks) H duplex (Morax Axenfeld) B diphtheriae P tularensis and M mallei (Glanders)

EPITHELIAL SCRAPINGS

Information of value is obtained from epithelial scrapings of the conjunctiva A platinum spatula is employed after local anesthetization The material is placed on a slide fixed with methyl alcohol for five minutes and stained with dilute Giemsa (1 drop to 2 cc of distilled water) The stain is kept on overnight at room temperature or for one hour in the incubator To bring out inclusion bodies the slides are passed momentarily through 95 per cent ethyl alcohol

a layer of gauze Cold compresses are especially useful in conjunctivitis (p 1616) Cold may be used in preference to heat in acute congestive glaucoma In iritis heat may aggravate pain and the use of cold for short periods is comforting

Infra red Rays—The infra red lamp is a simple and clean means of providing heat to the eye Applied to the closed lids no damage is done by infra red therapy Special lamps have been designed for eye work

Infra-red light from 13 000 to 16 000 Angstrom units is absorbed almost entirely by the cornea Large doses of infra red may produce cataract a possible explanation of the high incidence of this condition in India Large doses may cause permanent injury of the retina as illustrated by the macular lesion in solar eclipse blindness

Medical Diathermy—Short wave and electromagnetic diathermy have been tried on the eye Short wave diathermy may raise the temperature in the vitreous as high as 109° F The effect seems useful in *orbital cellulitis* and *chronic uveitis* Elevation of intra ocular temperature above 106° F has been reported to cause *thrombosis of the central retinal vein*

Surgical Diathermy—Surgical diathermy is most widely used in the operation for *retinal detachment* for permanent removal of cilia (often done by electrolysis) for correction of *entropion* and *ectropion* (Ziegler cautery operation) and for removal of small *chalazia* or *papillomas* of the lids In large *orbital tumors* electrocoagulation blocks avenues of extension and reduces bleeding

The Thermophore—The thermophore is a device designed to apply a measured amount of heat (145° F) directly to an ulcer of the cornea for a definite period of time usually one minute

Roentgen Ray and Radium Treatment—Roentgen therapy lies entirely in the province of the roentgenologist as cataracts damage to the lids and cornea and glaucoma may follow improper use The use of x rays or radium is indicated in the more diffuse types of *skin neoplasm* especially basal cell epitheliomas and those adherent to bone *Vascular nevi* about the lids are especially suited to radium treatment *Intra ocular tumors* do not respond very well to irradiation therapy but in conditions such as *bilateral gliomas* (p 1419) it is the only means available other than removing both eyes

Early deep hordeolum acute dacryocystitis early post traumatic or postoperative intra-ocular infection chronic blepharitis tuberculous iridocyclitis and choroiditis and thrombosis of the central vein of the retina may respond favorably to roentgen therapy

Grenz Rays—*The border rays described by Bucky are between the* ultraviolet and the longer roentgen rays in the spectrum measuring about 2 Angstrom units These rays have slight penetrating power and are believed incapable of producing the deleterious effects of roentgen rays Their efficacy is under investigation for the treatment of superficial corneal lesions and inflammations of the lids

Phototherapy—Local phototherapy with ultraviolet light is delivered by the Birch Hirschfeld lamp Its popularity has waned with the advent of other means of therapy and its main usefulness if any seems to be in *dendritic keratitis* and *superficial catarrhal ulcers*

The cornea absorbs almost all the ultraviolet rays below 2950 Angstrom units and the lens absorbs all the higher ultraviolet rays Corneal absorp-

accompanies early stages of infection or reactions to trauma Cold is best applied to the closed lids with pieces of cotton frequently changed from

TABLE 105—LOCAL APPLICATIONS OF LIDS AND EYES

Collyria	Physiological Saline 4 per cent Boric Acid
Astringent	0.2 to 0.3 per cent Zinc Sulfate or Copper Sulfate added to collyrium
Vasoconstrictor	Epinephrine 1 1000 added to collyrium in ratio of 1 10
Rubefacient	Ethylmorphine Hydrochloride (dionin) 5 to 20 per cent solution
Local anesthetic	Pontocaine ½ to 1 per cent Butyn 1 to 4 per cent Metycaine 2 to 4 per cent Holocaine (Phenacaine) 1 per cent Cocaine Hydrochloride 1 to 5 per cent Procaine 2 per cent
Protective	Petroleum Jelly Castor Oil
Bactericide	1 3000 to 1 10 000 Bichloride of Mercury Ointment for lids 2 to 3 per cent Ammoniated Mercury Ointment for lids 1 per cent Yellow Oxide of Mercury for lids 1 to 2 per cent Zinc Oxide Ointment for lids 5 per cent Sulfathiazole Ointment for lids Sulfanilamide Powder 30 per cent Sodium Sulfacetimide 2 per cent Tincture of Brilliant Green in 70 per cent alcohol for lids 10 per cent strong Silver Proteinate 25 per cent weak Silver Proteinate ¼ to 1 per cent Silver Nitrate 2 per cent Mercurochrome 1 or 2 per cent Ethylhydrocupreine Hydrochloride (optochin) Tyrothricin (0.3 per cent) Penicillin (1 cc equals 250 to 2000 units)
Miotics	1 to 2 per cent Pilocarpine Hydrochloride 0.5 to 1 per cent Physostigmine Salicylate (eserine) 2 to 5 per cent Neostigmine 5 to 20 per cent Acetylcholine 1 to 20 per cent Mecholyl 0.5 to 2 per cent Doryl 0.1 per cent Diisopropyl Fluorophosphate (DFP)
Mydriatics	5 to 10 per cent Eucatropine (Euphthalmine) ¼ to 3 per cent Atropine Sulfate 1 to 2 per cent Homatropine Hydrobromide 0.1 to 0.5 per cent Scopolamine Hydrobromide 1 per cent Amphetamine Sulfate ¼ to 2 per cent Neosynephrine 1 per cent Paredrine 3 per cent Ephedrine Sulfate 2 to 5 per cent Cocaine Hydrochloride
For staining cornea	2 per cent Fluorescein in 3 per cent Sodium Bicarbonate

a bowl of cracked ice Ice should never be applied directly to the lids If sterility must be observed cracked ice in a rubber glove is pl[illegible] over

orbit or globe *Diphtheria antitoxin* (p 310) is used in the rare instances of conjunctivitis due to *B diphtheriae* and has also been recommended in large doses (10 000 to 16 000 units) for *sympathetic ophthalmia* and in smaller doses (5 000 units) for *herpes zoster ophthalmicus* *Antimeningococcic serum* was used extensively in the ocular complications of epidemic *meningitis especially endophthalmitis* *Since the advent of antibiotics* its value has declined although it may be wise to combine the methods *Antipneumococcic serum* has been tried in ulcers of the cornea but is being superseded by sulfonamides *Transfusions of whole blood* from persons who have recovered from herpes zoster seem to prevent ocular complications and mitigate serious consequences after the disease is established

Vaccines—*In ophthalmology the chief use of vaccines has been in the* treatment of recurrent hordeola and severe blepharitis due to *staphylococci* *Autogenous vaccines* prepared so as to leave the bacterial proteins practically unchanged seem best It is advisable to start treatment with a minute intradermal injection (0 02 cc) to judge the patient s sensitivity to the toxins or bacterial proteins Later subcutaneous injections are given in amounts causing no marked local and certainly no focal or ocular reaction (p 80)

Gonococcal vaccine seems useful in gonorrheal iritis (p 1633) Autogenous vaccines prepared from foci of infection that cannot be entirely eradicated sometimes are of great benefit in corneal ulcers and uveitis

TOXOID—The importance of the exotoxins of staphylococci in the production of chronic blepharitis conjunctivitis and keratitis has stimulated the use of *staphylococcus toxoid* or weakened toxin in the digest modified form (Lederle) Dosage is based on the reaction to small intradermal injections (0 001 to 0 003 cc) Semi weekly injections are given with increasing doses (0 1 cc) depending upon the responses The maximal amount is 1 0 cc

Tuberculin—Tuberculin therapy is extensively used in ophthalmology especially by those who are unimpressed by the importance of focal infection In contradistinction to its uselessness in pulmonary tuberculosis it is considered an important factor in the treatment of *ocular tuberculosis* especially *sclerosing keratitis iritis iridocyclitis* and *chorioretinitis* In these special manifestations of the disease frank pulmonary tuberculosis is seldom present If active tuberculosis is present elsewhere in the body tuberculin therapy is contraindicated

TECHNIC—A *diagnostic series* of intradermal injections is carried out with very small doses of old tuberculin In a severe case the initial injection is *a control of saline followed by 0 000001 mg of O T The reaction* is read at twenty four and seventy two hours If negative stronger doses of 0 00001 mg and 0 0001 mg are tried Positive tests are of little diagnostic value but indicate the proper dosage for the initiation of therapy

Treatment with tuberculin is always of long duration particularly if an initially high sensitivity precludes all but minute doses at the onset Injections are usually given twice a week being gradually increased until 1 to 5 mg are tolerated without a reaction When a local reaction is encountered the next injection is the same as the previous dose which caused no reaction When a dose of 0 1 mg is reached the intervals are lengthened to one week

tion after exposure to ultraviolet light results in an *abiotic reaction* and an extremely painful *keratitis* Similar mechanisms are involved in *photophthalmia* or *snow blindness* and after accidental exposure to the flash of an *electric arc* *Treatment* consists of the instillation of epinephrine and a local anesthetic after which dark glasses are worn

Massage —Massage is useful in clearing the opacity that follows corneal ulceration in the maintenance of normal intra ocular tension in glaucoma especially after a filtering operation and in the treatment of *meibomitis* and *chalazia* (p 1611) In corneal ulceration, 2 per cent boric ointment is anointed and the eye is gently massaged by rubbing the closed lids with the forefinger In *glaucoma* the two index fingers are placed on the upper lid of the depressed eyeball each finger alternately is pressed in and released so as to indent the globe The massage is done thirty times and repeated two or three times a day

Iontophoresis or Galvanic Therapy —Using a dry cell battery (galvanic electricity) in a special apparatus medication can be administered to the eye in an ionized form increasing the concentration of the drug in the aqueous Iontophoresis with sulfanilamide and penicillin is of great help in corneal ulcers due to *B pyocyaneous* a condition in which treatment hitherto has been unsatisfactory as well as in conjunctival and other superficial infections

SYSTEMIC METHODS OF THERAPY

The useful methods of systemic therapy in ophthalmologic disorders include ultraviolet exposure elimination of foci of infection the administration of immune serums toxoids vaccines and tuberculin non specific foreign protein therapy hyperthermia specific chemotherapy with antiluetic drugs sulfonamides and the antibiotics such as penicillin and the use of vitamins and hormones

Ultraviolet Therapy —General ultraviolet irradiation produces a mild skin reaction and changes in the blood and tissues that resemble those of foreign protein shock *Tuberculous uveitis sclerokeratitis* and *phlyctenulosis* seem to be influenced favorably by irradiating one third of the body surface at one sitting and repeating three times a week for fifteen treatments General ultraviolet therapy has also been suggested for the treatment of *sympathetic ophthalmia*

Elimination of Foci of Infection —In ocular inflammations particularly those involving fibrous tunic and uveal tract (iritis iridocyclitis and choroiditis) a careful search is made for foci of infection *Tonsillar* and *nasal infections* play an important role in optic neuritis and in uveitis of younger people In older people *dental sepsis* is particularly important as a cause for uveitis and keratitis Dead teeth and retained roots are suspect and devitalized teeth require peri apical exploration even if roentgenograms are normal The *genito urinary tract* deserves investigation The possibility of an *intestinal focus* of infection must be considered

Biological Therapy —Biological therapy employs serums vaccines toxoid tuberculin and foreign protein

Serums—Immune serums are used only occasionally in ophthalmic treatment *Tetanus antitoxin* (p 297) is indicated after an injury in which material likely to contain tetanus spores is carried into the lids

phopathia venereum It also merits trial in Welch bacillus infection in uveitis of unknown origin and in Koch Week s conjunctivitis Little success has been experienced however in Morax Axenfeld infection or epidemic virus conjunctivitis

Untoward ocular reactions that follow systemic sulfonamide therapy include transient myopia edema of the lids chemosis and allergic conjunctivitis retinal hemorrhages optic neuritis and mydriasis

Penicillin—Penicillin like sulfonamide may be used locally or systemically in ophthalmic infections For topical application it is employed in a strength of 250 to 10 000 units per cc with concentrations augmented by iontophoresis (p 3792) Penicillin may be injected directly into the aqueous by the ophthalmologist The systemic introduction is accomplished by intramuscular or intravenous injection (p 106)

Penicillin has certain advantages over the sulfonamide drugs despite the fact that local sensitivity to the ointment may occur infrequently Direct injections of penicillin into aqueous are highly recommended in penetrating wounds and metastatic abscess It is also worthy of trial in anaerobic diphtheritic and spirochetal invasions The effects of systemic administration in gonorrheal ophthalmia are truly miraculous

In the treatment of coccal infection there seems no question as to the lesser irritation and better results of penicillin as compared to sulfonamide Ambulatory patients must be treated by topical instillation but those who are hospitalized or accessible to nursing service may be given intramuscular injections In the virus infections penicillin is inferior to the sulfonamides particularly sulfanilamide

Penicillin has prophylactic value in the management of ocular injuries and in intra ocular surgery It is given in large doses in orbital cellulitis where parenteral administration is supplemented by topical application of a solution containing as high as 10 000 units to the cc A suitable ointment for the treatment of blepharitis styes and furuncles is improvised by the addition of 250 to 500 units to each gram of 25 per cent petroleum jelly with 75 per cent cold cream

Tyrothricin—Concentrations of 5 to 33 mg per 100 cc of tyrothricin appear to be effective against gram positive organisms particularly pneumococci staphylococci and streptococci The suspension can only be employed locally since systemic administration is fraught with danger

Streptomycin—Streptomycin locally or systemically may prove of great value in the treatment of conjunctivitis due to *H influenzae* Koch Weeks and Axenfeld bacilli *P tularensis M tuberculosis* and *M leprae*

Hormone Therapy—Thyroid extract (p 1189) has been employed in myopia keratoconus and chronic uveitis without any definite evidence of success In parathyroid tetany which is often accompanied by cataracts the early administration of parathyroid hormone (p 1223) may prevent the development of cataracts or stay their progress if lens opacities have already developed Insulin (p 1237) is of value in the treatment of ocular complications of diabetes Despite enthusiastic claims of its value in glaucoma and myopia cortin injections (p 1267) have proved most disappointing

Vitamin Therapy—Vitamin A is definitely indicated in keratomalacia a true nutritional necrosis of the cornea It also is recommended for kerato

Foreign Protein—Foreign protein therapy has been successfully employed in the treatment of a variety of ophthalmic conditions including acute conjunctivitis gonorrheal ophthalmia, phlyctenular keratitis interstitial keratitis corneal ulcer acute and chronic iritis uveitis postoperative iridocyclitis scleritis sympathetic ophthalmia retinitis choroiditis optic neuritis retinitis pigmentosa herpes zoster and acute trachoma

Reactions may be produced by injections of boiled milk typhoid vaccine or the malarial parasite Milk is prepared by boiling for four minutes and cooling For the adult intramuscular injections of 8 to 12 cc are employed while 1 to 2 cc suffice for the infant With typhoid vaccine the H antigen is given in an initial intravenous dose of 10 000 000 and the amount is increased until a febrile reaction approximating 103° to 104° F has been accomplished In malarial therapy 5 to 10 cc of blood are taken from an infected donor suffering from the benign tertian variety The malarial blood is injected into the vein of the recipient who is then permitted to have 8 to 12 chills after which the paroxysms are terminated by the administration of quinine sulfate 0 6 gm (10 grains) given three times daily for five to seven days (p 517)

Hyperthermia—In addition to fever therapy using foreign protein typhoid vaccine and malarial parasites hyperpyrexia may be effected by the inductotherm or the hypertherm (p 3789) These technics are specialist province and are not to be attempted except under institutional supervision Principal indications are interstitial keratitis and optic atrophy of syphilitic origin

Specific Anti infective Therapy—Tremendous strides have been made in the anti infective therapy of ophthalmic infection The practitioner has access to sulfonamides penicillin streptomycin and tyrothricin The first three of these may be used topically or systemically tyrothricin however is only available for topical application

Sulfonamide—The available sulfonamide drugs for local application include 5 per cent sulfathiazole application of sulfanilamide powder and 30 per cent solutions of sodium sulfacetimide (p 88) The disadvantage of the local use of the sulfonamides is the frequent production of contact dermatitis of the lids allergic conjunctivitis increased tendency to opacification of the cornea delayed healing and increased scarring The advantages of local therapy are the lesser hazards of producing toxic systemic manifestations

The systemic use of the sulfonamides results in the appearance of the drug in the aqueous Sulfanilamide and sulfadiazine appear in the highest concentrations sulfapyridine is intermediate and sulfathiazole is least well excreted Those who favor the systemic method of therapy contend that benefits produced by topical methods are dependent upon absorption into the general circulation with re excretion into the aqueous They do not believe that bacterial antagonism is produced as the result of direct action of locally applied drug

Whether used locally or systemically however there is general agreement that the great value of the sulfonamides is in the treatment of gonococcal pneumococcal meningococcal staphylococcal and streptococcal infection Sulfanilamide appears to be of demonstrable if not specific value in the virus infections of trachoma inclusion conjunctivitis and lym

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conjunctivitis sicca epithelial dystrophy recurrent catarrhal ulcers and asthenopia associated with photophobia

Thiamine chloride appears to be of great value in toxic amblyopia due to alcohol and other forms of optic neuritis Deficiency of riboflavin is believed to cause a peculiar keratitis associated with vascularization of the cornea Rosacea keratitis is said to clear rapidly on adequate doses of riboflavin Its use is also suggested in attempts to influence the course of senile cataracts

Ascorbic acid is indicated in diabetic retinopathy intra ocular hemorrhages and the treatment of senile cataracts *Viosterol* is advised in phlyctenular keratitis but has no definite valuable effect in myopia

MINOR SURGERY

Much of the minor surgery of the eye must necessarily be done by the practitioner The more complicated procedures however merit reference to the specialist ophthalmologist

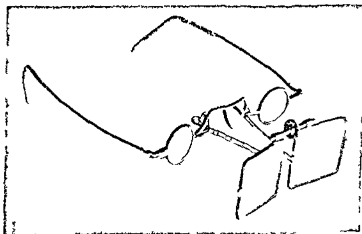


Fig 296 —Binocular magnifier *

Instruments —Procedures involving the eye require a *cilium forceps* and a loupe magnifier to assist in the detection and removal of foreign bodies (p 1572) in addition to the minor surgery kit

Application of Silver Nitrate to the Lids —After local anesthetization an applicator moistened with 1 per cent silver nitrate is rubbed briskly over the lid margin and cilia An attempt is made to remove scales and penetrate into the *underlying ulcerations To alleviate the sting* a drop of epinephrine is instilled into the conjunctival sac

Application of Silver Nitrate to the Conjunctiva —After anesthetization an applicator is moistened with 1 per cent silver nitrate and gently touched, but not rubbed on the conjunctiva of upper and lower lids After waiting several minutes the conjunctival sac is irrigated with salt solution If the eyes remain irritated the patient applies cold compresses for five minutes and a drop of *epinephrine is instilled to relieve residual* smarting

* Gifford Textbook of Ophthalmology

Application of Copper Sulfate in Chronic Conjunctivitis and Trachoma—After anesthetization the copper sulfate stick is touched gently to two or three places on the lower lid The eye is then treated as after the application of silver nitrate Copper treatment is very irritating at first but the patient achieves a tolerance to repeated applications

Manual Expression of the Lids—Manual expression of the lids is of value in *blepharitis* (p 1609) *meibomitis* (p 1613) and *chalazia* (p 1611) in their incipient stages One thumb is placed on the lower lid the other on the upper lid and the two lids are squeezed together to express secretion

Removal of Cilia—Removal of cilia is done for *trichiasis* (p 1569) *distichiasis* (p 1569) and the abortive treatment of *styes* (p 1610) A special cilium forceps is required as lashes are so fine that they often slip through the best forceps Breaking the lash in the middle may aggravate discomfort and make removal almost impossible

Rupture of Cysts of the Lid Margin.—Cysts of the lid margin (p 1566) may act as foreign bodies They are easily ruptured with a wooden applicator or the tip of a sharp scalpel

Removal of Foreign Bodies from the Upper Lid—To evert the upper lid the patient is instructed to look down The physician grasps the lashes with the left hand and pull the lid up while exerting counterpressure with a cotton applicator on the upper lid just above the upper tarsal border (*i e* 7 to 8 mm above the lid margin)

Once the lid is everted the foreign body (p 1572) is usually apparent and is removed with a moistened cotton applicator If none is seen folds in the tarsus are explored with the applicator Foreign bodies are not always black but may be any color so that any suspicious object even if flesh-colored is touched to see if it is removable If *lithiasis* or *calcific yellowish deposits* (p 1566) of the conjunctiva scratch the cornea they must be removed in the manner of foreign bodies After instillation of a few drops of anesthetic they are picked off with a sharp pointed knife or a hypodermic needle

After removal of the foreign body *fluorescein* is instilled and washed out Injured corneal epithelium stains green and this is sufficient reason to require the application of a dressing

Application of the Eye Dressing—When corneal epithelium is injured a *patch* must be applied until the cells no longer stain with fluorescein Sulfathiazole ointment (5 per cent) is instilled in the conjunctival sac and a piece of moistened gauze or woven cotton material is placed over the closed lids to prevent loose dry cotton which is then placed on top of this from scraping the cornea The dressing is held in place by 1 inch adhesive strips or by Scotch (cellulose) tape The adhesive is applied in a diagonal direction so that it ends on the malar bone and does not interfere with chewing If a pressure dressing is desired gauze is used instead of cotton and 1 inch wide strips of adhesive are applied

If a *continuous wet dressing* is desirable as in acute dacryocystitis or an abscess of the lid the cotton is replaced by gauze moistened with penicillin sulfanilamide boric acid or saline This may be covered with waterproof tissue and held in place by a 1½ inch bandage The first few turns of the bandage are placed horizontally around the head under the occiput They are then brought up under the ear to cover the eye after which

they are wound around the head At the meeting of the diagonal and horizontal portions the bandage is tied with small vertical strips of gauze or adhesive, similar ties are made above and below the ear

Removal of Corneal Foreign Bodies—It is advisable to refer the patient with a corneal foreign body especially of the imbedded metallic type to the ophthalmologist If this is not feasible the patient is placed in recumbency and is ordered to fix both eyes on some landmark on the ceiling With adequate light best obtained by focal illumination and local anesthesia a black or white foreign body can usually be removed with a moist cotton applicator A brown appearance suggests that the imbedded metallic foreign body has oxidized or rusted and a fine *hypodermic needle* is required for removal Although it is necessary to remove the rust as completely as possible damage to the cornea may result in *destruction of Bowman's membrane* with resultant *permanent opacity* If all the rust is not removed liquefaction of the involved area may occur within a week or so the rusted portion then sloughs out and a serious ulcer is produced

After the foreign body has been removed penicillin solution is instilled sulfathiazole ointment is applied and the eye is covered with a patch In a rust ring foreign body there usually is considerable iritic irritation and mydriasis is accomplished with 2 per cent homatropine provided there is no evidence of increased intra ocular tension (p 1526) The dressing is changed daily until complete healing is evidenced by failure to obtain a staining reaction with fluorescein

Incision of a Hordeolum—Anesthesia is not necessary for external incision of a *hordeolum* (p 1610) Using a sharp pointed knife an incision is made horizontal or parallel to the lid margin where the lesion points Pus is evacuated by mild expression if necessary

Removal of a Chalazion—The area of the chalazion (p 1611) is blocked off proximally by infiltration through the skin with procaine The injection then is extended down to the lid margin The lid is everted a few drops of anesthetic are instilled into the conjunctival sac and additional procaine is injected subconjunctivally just proximally to the tarsus in the region of the chalazion A special chalazion clamp is applied to expose the lesion and render the area bloodless The chalazion is incised through the conjunctival surface of the lid by means by a vertical incision If it is firm the granulomatous tissue is dissected with a scissors otherwise it is scooped clean with a curette An attempt is made to save as much of the conjunctiva as possible The incision is best left unsutured If the chalazion points through the skin a horizontal incision is made through the skin which must be carefully sutured at the end of the operation A dressing is applied for one day unless the skin is sutured in which case it is maintained for three to four days Skin sutures are removed after four days

Repair of Lacerations of the Lid—Repairs of lacerations of the lids (p 1571) especially those involving the margins or associated with avulsion at the medial canthus are procedures for the specialist Suture of a laceration of the lid may be followed by subsequent deformity It is better to delay suture of a laceration than to do a hasty and improper approximation Careful apposition of fragmented pieces is required using numerous thin silk sutures Unless great pains are taken with a torn lid margin notching occurs Sutures tied on the conjunctival side of a through and

through lid laceration may cause damage and ulceration of the cornea. The application of a firm pressure dressing is as important as the suture.

Cauterization of Corneal Ulcers.—After thorough anesthetization a fine applicator is moistened with a mixture of equal parts of *Tincture of Iodine* and *Glycerin* and applied to the ulcer until the area stains brown. Applications of *carbolic* or *trichloracetic acid* are the province of the specialist. Permanent opacification due to a chemical burn need not be feared from the iodine glycerin mixture which does not drip and run over. Atropine drops (1 per cent) are applied, an anesthetic ointment is spread on and a firm dressing is applied.

OPHTHALMIC SURGERY

In this brief review of the scope of ophthalmic surgery only broadest principles are described for the guidance of the general practitioner.

Probing of the Lacrimal Passages.—Probing of the lacrimal passages is a specialist office procedure done for obstruction or stenosis of the lacrimal passages (p 156). Performed gently after preliminary instillation of 2 per cent procaine or 5 per cent cocaine in the lacrimal sac the procedure is not very painful. One successful probing may relieve the condition. If hemorrhage occurs when an adhesion is broken new adhesions may form and perpetuate the obstruction. In infants with a congenital obstruction (p 1560) probing of the lacrimal passages under general anesthesia is generally very successful although the benefits may not be obvious for several weeks following the operation.

Incision of the Lacrimal Sac.—Incision of the lacrimal sac is done for *acute dacryocystitis* (p 1614). General anesthesia is required and after treatment is that of any other abscess.

Dacryocystectomy.—Extirpation of the lacrimal sac is performed under local anesthesia for *chronic purulent dacryocystitis* (p 1614). Hospitalization after the operation is brief. The patient wears a dressing over the affected eye for one week. This procedure removes a serious focus of infection and helps clear up tearing by the relief of coexisting conjunctivitis. Persistent postoperative tearing is a serious objection to its performance. Ophthalmologists are confining this procedure increasingly to older people.

Dacryocystorhinostomy.—In this operation instead of removal of the sac an incision is made in its medial wall which is then anastomosed to the nasal mucosa after a portion of the bony wall of the nose has been removed. A permanent opening is established between tear sac and nasal cavity. The procedure is done under local or general anesthesia and is rapidly becoming the method of choice except in people of advanced age. It is a considerably more formidable procedure than dacryocystectomy and requires hospitalization for five to seven days. Symptoms are alleviated and tearing stops in 80 per cent of cases.

Extirpation of the Accessory Lacrimal Gland.—If tearing continues after dacryocystectomy removal of the accessory lacrimal gland is advised. The operation is done under local anesthesia.

Plastic Operations on the Lids.—Plastic operations on the lid include some of the simplest and most complicated procedures in ophthalmology. The results are usually good except when extensive reconstructive surgery is required. The latter are best performed by an ophthalmologist specializing in plastic surgery. Even in the best hands however repeated failures occur time and again and the surgeon must have considerable patience to achieve a final good result.

Ptosis Operations.—Ptosis operations are usually performed on small children. Proper procedures yield results that are usually eminently satisfactory.

Keratoplasty.—Transplantation of cornea have been successfully performed by specialists for restoration of vision in patients whose vision was lost due to extensive corneal opacities (p 1628). A graft of clear cornea is taken from an eye removed for another cause or from a cadaver specimen. The graft usually takes and may remain clear enough to improve the patient's vision considerably.

Tattooing of the Cornea.—A blind eye with an ugly obvious corneal opacity may be made less unsightly by tattooing the opacity to resemble the normal pupil. Even in eyes with some vision this procedure is often indicated and produces gratifying cosmetic results.

Extraction of the Senile Cataract.—Extracapsular extraction of a cataract (p 159) con

sists in opening the capsule of the cataractous lens and expressing its contents leavin the capsule in the eye The *intra capsular method* removes *capsule and lens at* one time The *extracapsular method* is somewhat easier and safer but an after cataract may form requiring *discission* (*needling*) at a later date

A successful intracapsular extraction gives a clear black pupil and no discission is required its major drawbacks are greater danger loss of vitreous and resultant chroni uveitis which may terminate in ultimate loss of the eye Either method in *expert hands gives highly* gratifying results in the large majority of instances The operations are done under local anesthesia

Intra and extracapsular extractions are preceded by careful preoperative surveys especially for focal infection oral sepsis diabetes and hypertension The patient remains in the hospital ten to fourteen days after operation Often a preliminary *iridectomy removing a* portion of the iris to form a keyhole pupil is performed After this operation the patient stays in the hospital for five days and returns two months later for the cataract extraction

Preliminary iridectomy is particularly advisable in patients with *hypertension* or *diabetes* In the pre- and postoperative care of the diabetic patient most ophthalmic surgeons limit the diet drastically rather than us insulin which they feel increases the tendency toward intra ocular hemorrhage

Discission of Secondary (After) Cataracts—If a membrane occurs following a cataract extraction and interferes with vision it may b incised or needled so as to effect a clear central opening This procedure requires only one or two days hospitalization Sometimes a more extensive procedure is necessary if the membrane is thick and tough

Discission of Congenital Cataracts—Discission of the congenital cataract (p 1594) requires that the capsule be incised in a number of places to allow free ingress of aqueous In time the soft cataract completely dissolves but a membrane may rema n and demand a second discission The disci sion procedure is performed also for traumatic cataract in persons under the ages of twenty five to thirty years After that time the lens contains a nucleus which will not dissolve

Removal of Intra Ocular Foreign Bodies—A metallic intra ocular foreign body (p 1572) may be removed by a strong *magn t* applied to the eye An attempt is made to draw the substance into the anterior chamber from which it is removed after incision by means of a smaller magnet If the foreign body is nonmagnetic the problem is more difficult if an incision is made beyond and behind the lens considerable vitreous may be lost with the later danger of retinal detachment and loss of the eye by infection If magnetic bodies such as steel are not removed the eyeball will eventually degenerate (*siderosis bulbi*) Any intra ocular foreign body poses the hazard of *sympathetic ophthalmia* (p 1569)

Iridectomy for Acute Glaucoma—In acute glaucoma (p 1581) an incision is made into the eye in the angle of the anterior chamber 1 to 2 mm behind the limbus and a broad basal iridectomy is performed A good piece of iris is abscised at its root to facilitate drainage between anterior and posterior chambers The resultant defect in the iris gives the appearance of an inverted keyhole This operation is generally successful and when properly performed usually relieves the condition permanently

General anesthesia is sometimes preferred because the acute congestion of the eye results in poor absorption of the locally applied anesthetic

The Elliott Trephine Operation—The Elliot trephine operation is most commonly used for *chronic simple glaucoma* (p 1578) A small opening is made at the limbus to effect a permanent drainage between anterior and posterior chambers and conjunctiva This is an eminently successful maneuver and the eye continues to function well for a number of years Sometimes however a conjunctival bleb covering the trephine opening becomes edematous and infected Until the advent of sulfonamides this complication resulted in loss of the eye With modern chemotherapy the trephine bleb infection can be successfully combated

Lagrange Operation—The Lagrange operation is done for *secondary glaucoma* (p 1581) A portion of *sclera* is removed in addition to a basal *iridectomy*

Cyclodialysis—Cyclodialysis is often p rformed for *glaucoma* following cataract extraction (p 1581) The ciliary body is separated from the adjacent sclera with little trauma to the eye

Retinal Detachment Operations—The separated retina (p 1573) rarely reattach s spontaneously Until recently retinal detachments usually resulted in degeneration of the eye and secondary cataract formation

Present operative procedures which result in successful reattachment in at least 60 per

cent of patients consist of locating the retinal tear and surrounding it by a barrage of *diathermy punctures* in order to set up an *adhesive choroiditis* Postoperative care is more of an ordeal than the operation itself Both eyes must be bandaged to avoid movement the patient must remain flat in bed for at least two weeks Even after the dressings are removed glasses are worn to permit vision only through small central perforations

Operations on the Extra Ocular Muscles—Operative procedures are devised to *strengthen a muscle* by cutting off a piece reattaching the shortened muscle to its original insertion or advancing forward the insertion To *weaken a muscle* it is recessed the insertion is placed somewhat behind the original position or it is tenotomized or cut off from its insertion The last method may result in an overcorrection

Successful muscle operations depend on careful preoperative study and clean operative technic to prevent the formation of adhesions which may nullify the procedure The patient is warned in advance that a second operation may be necessary as it is far wiser to do a little less than to undertaken too much and overcorrect the condition

In children general anesthesia is usually employed but in adults local infiltration is preferable The operated eye is bandaged for four or five days and good cosmetic results are usually achieved

Enucleation of the Eye—The removal of an eye is a simple but harrowing procedure The implantation of a gold glass or plastic ball inside Tenon's capsule requires most careful surgery The operation is done under local anesthesia and the patient is not required to stay more than a day or two in the hospital unless an implant is performed

Exenteration of the Orbit—Exenteration of the orbit is required for *malignant orbital tumors* (p 1566) This very extensive procedure is not complete without the removal of everything in the orbit including periosteum

CHAPTER 76

THE EYE CONGENITAL ABNORMALITIES ANALOGUES OF THE DERMATOSES CYSTS AND NEOPLASMS

CONGENITAL ABNORMALITIES

CONGENITAL abnormalities of the eye are usually clearly visible by direct inspection or by ophthalmoscopy (p 3628) Their recognition requires the practitioner to summon the specialist since certain of the anomalies are amenable to correction by methods of plastic surgery

CONGENITAL ANOMALIES OBSERVED BY INSPECTION

Albinism

Congenital absence of pigment Brows and lashes white Conjunctiva hyperemic Iris pale Pupil red Orange red fundus Optic disk almost indistinguishable High myopia Nystagmus Poor vision

Anophthalmos

Absence of eye due to failure of primary optic vesicle to bud from the cerebral vesicle

Blue Sclerotics

Associated with *fragilitas ossium* (osteogenesis imperfecta) multiple fractures and deafness (p 2879)

Buphthalmos

Ox like enlargement of globe due to obstruction to drainage of intra ocular fluid Intra ocular tension rises with *congenital glaucoma* Vision subnormal and optic atrophy may occur

Coloboma (Fetal Fissure)

Keyhole appearance of iris Defect of lens Pale white area due to defect of choroid and retina with a border of black pigment Branches of retinal vessels run across coloboma If optic nerve is involved large excavation appears usually on inferior aspect

Coloboma of Lids

Triangular notch of lid margins with absence of lashes and glands

Congenital Miosis

Absence of dilator muscle

Congenital Mydriasis

Absence of sphincter muscle

Corectopia

Anomalies in position of pupil

Corneal Opacities

Often associated with anterior synechia

Cyclops

Single eye in middle of forehead

Dermoid (p 1566)

At limbus in cornea or on conjunctiva Yellow flat oval tumor May contain hairs

Dermolipomas

Small yellow tumors in deep conjunctival tissues usually between superior and external recti

Distichiasis (p 1569)

Meibomian glands replaced by second row of incurving lashes



Fig 297 —Congenital coloboma of eyelid



Fig 298 —Epicanthus

Dyscoria

Slit shaped pupil as in cat

Embryotoxon

Annular opacity of periphery of cornea Continuous with sclera as contrasted with arcus senilis which has outer clear ring of cornea

Epicanthus

Bilateral skin fold projects over and partially covers inner angle of eye Normal in Mongolians

Epitarsus

Apron like fold of conjunctiva attached to inner tarsal surface of lid May be associated with congenital ectropion

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Corectopia

Anomalies in position of pupil

Corneal Opacities

Often associated with anterior synechia

Conus or Inferior Crescent

Crescentic white area usually situated just beneath an elliptic distorted nerve head Condition non progressive as differentiated from myopic conus which is situated temporally

Cysts of Retina

Rare rounded tumors

Detachment of Retina

Rare anomaly (p 1573)

Ectopia Lentis

In association with arachnodactyly (elongation of bones of hands and feet) in Marfan s syndrome

Lenticonus

Elongated lens and visual distortion

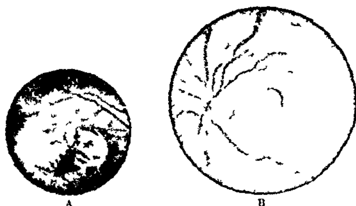


Fig 300 — A Coloboma of the macula B Medullated nerve fibers

Macular Coloboma

Large horizontal oval or round defect in macular region Stretched sclera seen on floor with black pigment *Retinal vessels* pass over area Considerable visual *defect and nystagmus*

Medullated Nerve Fibers

Striated white patch *in superficial retinal layers covering the vessels* in whole or part Characteristic frayed and feathered edge resembling shaving brush Partial scotoma may be caused by opaque character of medullated sheaths but usually no visual impairment

Melanosis Bulbi

Increase of pigment of uveal tract sclera iris and/or fundus

Melanosis of Retina

Grouped pigmented areas scattered through retina

Microphakia

Small lens

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Heterochromia
Color of irides differs

Megalocornea
Bilateral enlargement of anterior segment of eye Large refractive error

Microcornea
Cornea abnormally small in an otherwise normal eye Vision may be normal Tendency to glaucoma

Microphthalmos
Small eye which may be normal Usually associated with maldevelopment of retina and impaired vision Glaucoma often present

Polycoria
Two or more pupillary openings



Fig 299—Congenital ptosis in mother and son associated with almost complete external ophthalmoplegia *

Ptosis (p 1649)
Drooping of upper lid May be unilateral or bilateral

Stenosis of Nasolacrimal Ducts (p 1569)
Tearing and chronic dacryocystitis in infants

CONGENITAL ANOMALIES OBSERVED BY OPHTHALMOSCOPY

Aphakia
Absence of lens

Cataract
See p 1592

Choroideremia
Absence of choroid and pigment epithelium of retina Red reflex only in macula while rest of fundus is gleaming white *Night blindness* and concentric contraction of visual fields but normal color perception

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Oguchi s Disease

Congenital night blindness in Japanese

Persistence of Hyaloid Artery

Fine green gray cord extending from nerve head through central vitreous to posterior aspect of lens May have fine glial mantle May be complete or partial

Persistent Pupillary Membrane

Complete or partial remains of anterior part of vascular sheath of lens No interference with vision

Pigmentation of Optic Nerve

Spotty or uniform deposits

Pseudoneuritis

Heaping up of nerve fibers on optic disk with indistinctiveness of margins of disk and elevation of the nerve head resembling optic neuritis and papilledema Differentiate from *pathological* conditions by the fact that it is non progressive no hemorrhages or exudates are present arteries are not narrowed and veins are not engorged Usually but not invariably found in hyperopic eyes

Retinal Folds

Tent like ridges of retina project into vitreous Stretch from infero temporal portion of nerve head to periphery of retina May end at posterior aspect of lens producing cataractous change

Treatment —Confronted with a congenital anomaly of the visual organs it is the duty of the practitioner to refer the patient to the consultant ophthalmologist for expert opinion concerning prognosis and therapeutic possibilities Prophylactic measures against glaucoma (p 1578) are of value in *microphthalmos* and *buphthalmos* minor surgical procedures may be useful in *epitarsus* and *epicanthus* *dermoids* and *dermolipomas* are re moved for histological study the incurving lashes in a *distichiasis* should be epilated *stenosis of the nasolacrimal ducts* may respond to dilatation (p 1569)

ANALOGUES OF THE DERMATOSES

The skin of the eyelids often participates in the dermatoses Addition ally there may be involvement of conjunctiva cornea and sclera in cer tain of the more serious involvements of the skin

Acanthosis Nigricans (p 3357)

Conjunctivitis with papillary hypertrophy

Acne Rosacea (p 3357)

Blepharo conjunctivitis keratitis and episcleritis

Contact Dermatitis (Eczema) (p 3330)

Local drugs such as sulfonamides atropine anesthetics and mercury *Cosmetics* such as mascara nail polish nail dyes hair washes and rinses dyes rouge powder and lipstick

Dermatitis Herpetiformis (p 3371)
Conjunctival vesicles erosions xerosis keratinization and symblepharon (p 1569)

Epidermolysis Bullosa (p 3151)
Conjunctival vesicles corneal scarring ulcer and perforation



Fig 301 —Atropine dermatitis



Fig 302 —Pemphigus of conjunctiva with symblepharon

Erythema Multiforme (p 3374)
Catarrhal or purulent conjunctivitis corneal ulcers with perforations and phthisis bulbi associated with stomatitis and rash as *Stevens disease*

Hydroa (p 3176)
Severe conjunctivitis and keratitis

Ichthyosis (p 3152)
Chronic catarrhal conjunctivitis and keratitis

Lichen Planus (p 3389)
Rare involvement of conjunctiva and cornea

CHAPTER 77

THE EYE INJURIES FROM MECHANICAL, PHYSICAL AND SYSTEMIC CAUSES

MECHANICAL DISTURBANCES

THE simpler mechanical disturbances of the eye are easy of recognition They require prompt reference to the specialist for the initiation of technical forms of therapy mostly in the nature of plastic surgery The required procedures often are simple of execution The risks of operation are minimal and the clinical results are highly satisfactory from the standpoint of cosmetic appearance and the prevention of ocular complications

Treatment—*The majority of mechanical disturbances require reference* to the specialist Plastic surgery may be of great value in ankyloblepharon blepharophimosis entropion eversion of the lacrimal punctum ptosis trichiasis and symblepharon Lagophthalmos may be improved by a tarsorrhaphy Dilatation and irrigation of the canaliculus is sometimes of value in occlusion of the lacrimal punctum For deficient lacrimation large doses of vitamin A and the instillation of Ringer s solution may be tried *with surgical closure of the tear puncta if non operative treatment fails*

INJURIES

The eye is vulnerable to many types of injuries particularly in modern industrial life Many carry serious threat of permanent damage to the visual apparatus and the practitioner is required to seek *specialist consultation* on frequent occasions There are few human tragedies which approach the horror of *sympathetic ophthalmia* (p 1569) in which loss of the traumatized eye is followed by destruction of the seemingly uninjured organ

The following chart deals briefly with the common ophthalmological injuries It is *followed immediately by more lengthy discussions of sympathetic* ophthalmia and the more serious injuries and mechanical afflictions of the visual apparatus

Treatment—Except for the extremely superficial injuries trauma to the eye requires reference to the specialist The practitioner should confine his efforts to the determination of underlying pathology and to symptomatic treatment Films of the skull and orbit are indicated with all mechanical *injuries especially those accompanied by emphysema* indicating communication with nose or accessory nasal sinuses

Symptomatic treatment consists of the application of compresses and the use of a pressure dressing until the patient may be seen by the ophthalmologist In the presence of perforating injuries it may be a wise precaution to initiate antibiotic treatment (p 106) with oral doses of *sulfadiazine and/or intramuscular injections of penicillin*

TABLE 107—MECHANICAL DISTURBANCES OF THE EYE THEIR ETIOLOGY AND CLINICAL MANIFESTATIONS

Lesion	Etiology	Clinical Manifestations
Ankyloblepharon	After burns and ulcers	Adhesion of upper [illegible]
Blepharophimosis	*Chronic conjunctivitis* (p [illegible])	*Contraction of palpebral f[illegible]* [illegible] cantbu[illegible]
Deficient lacrimation	Congenital absence of glands Occlusion of ducts of gland Trachoma Vitamin A deficiency (p 616) Paralysis of C N and VII	Keratoconjunct[illegible] [illegible] dryness and [illegible]
[illegible]	*Spastic* in young *Paralytic* with *weakness of orbicularis Senile* with relaxation of skin *Cicatricial* after wounds operations burns and ulcers	Exposure of lacrimal punctum with tearing Redness of exposed membranes Desiccation of cornea Keratitis [illegible] (p 16[illegible])
Entropion	*Spastic* in elderly Cicatricial after trachoma burns injuries or operations on lids	Trichiasis Corneal irritation Photophobia Corneal ulceration [illegible] opacities
Eversion of lacrimal punctum	Relaxed lids in senility ectropion *facial palsy* (p 1481) [illegible] *conjunctivitis*	[illegible]
Lagophthalmos	[illegible] (p [illegible]) [illegible] of lid from burns or operations With ectropion or facial palsy (p 1481) In [illegible] and comatose	Incomplete [illegible] of palpebral fissure Exposure of cornea with keratitis [illegible] (p 16[illegible]) Corneal opacities and ulceration Corneal perforation and panophthalmitis (p 15[illegible])
Occlusion of lacrimal puncta	Congenital Acquired from foreign body eyelash streptothrix concretion adhesions after inflammation	Punctum swollen Canaliculus [illegible] Pressure produces thin pus which [illegible] contain [illegible]
[illegible]	Congenital or acquired (p 1649)	*Droop of upper lid Congenital* [illegible] lateral oculomotor [illegible]
Trichiasis	Follows blepharitis injuries burns and trachoma (p 16[illegible])	Inverted [illegible] irritate cornea
Symblepharon	After [illegible] burns and ulcers	Adhesions between [illegible]

SYMPATHETIC OPHTHALMIA

In sympathetic ophthalmia serous or plastic inflammation of the uveal tract of one eye follows a similar inflammatory process in the other In most instances the lesion in the exciting eye is a traumatic iridocyclitis due to a perforating injury in the region of the ciliary body The ophthal

mia in the 'sympathizing eye arises no sooner than three weeks following the injury to the exciting eye and it may be delayed for several years

Not all perforating injuries involving the ciliary body result in sympathetic ophthalmia Unfortunately however there is no way of determining which will result in this tragic occurrence and which will not

Clinical Manifestations —Following injury to the exciting eye the sympathizing eye becomes irritable and exhibits photophobia lacrimation pain and dimness of vision Examination discloses the presence of iridocyclitis of the exciting eye The sympathizing eye at first reveals nothing but tenderness over the ciliary region later irritative symptoms develop progressively or intermittently Under best circumstances the sympathetic iridocyclitis entirely disappears but in less favorable instances inflammatory signs develop and these may terminate in blindness Objective manifestations of sympathetic iridocyclitis include circumcorneal injection the presence of punctate deposits upon the posterior surface of the cornea (k p) miosis and increased intraocular tension the iris becomes thickened its markings are obliterated and extensive posterior synechiae develop plastic exudate fills up the pupil and the anterior chamber becomes



Fig 304 —Senile ectropion



Fig 305 —Symblepharon with pseudopterygium result of lime burn *

shallow opacities are demonstrable in the vitreous and the lens becomes opaque there may be final detachment of the retina and shrinking and atrophy of the eyeball

The mechanism by which sympathetic ophthalmia progresses is unknown The hypotheses which have been advanced include spread of infection from the sheath of one optic nerve to the other irritation of ciliary nerves action of a toxin generated by bacteria metastases through the blood stream of pathogenic bacteria or an allergic phenomenon

Treatment —Failure to enucleate or remove the exciting eye may result in blindness of the sympathizing eye Hence prophylactic removal of the sightless injured eye is the recommended procedure Once a sympathetic ophthalmia has become established removal of the exciting eye has no value and may be contra indicated if it possesses even slight vision

The ophthalmologist is faced with a difficult responsibility since he has no definitive method by which he can determine whether sympathetic ophthalmia will develop and the extent of blindness that will ensue Since there is a breathing spell of three weeks between injury and onset of

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sympathetic ophthalmia the practitioner has ample opportunity for obtaining several expert opinions before final action is taken. In the mean

TABLE 108.—INJURIES OF THE EYE. THEIR ETIOLOGY AND CLINICAL MANIFESTATIONS

Lesion	Etiology	Clinical Manifestations
Birth injury to cornea	After forceps delivery	Rupture of Descemet's membrane may result in permanent opacities
Contusion of retina (commotio retinae)	Blunt injury to eyeball	Impairment of vision with central scotoma. Localized retinal edema at macula. Milky appearance. May clear completely or leave pigmented scar with permanent visual loss
Ecchymosis of lids	Local injury. Fracture of base of skull (p. 1450)	Black eye
Emphysema of lids	Fracture of orbital walls. Communication with nose or accessory sinuses	Crepitus
Erosion of cornea	Scratches by nail, edge of paper or twigs	Denuded area stains green with fluorescein (p. 1518)
Injuries to optic nerve	With skull fracture (p. 1450)	Usually loss of vision and optic atrophy after 4 to 6 weeks
Insect bites of lids		Considerable edema
Perforating injuries	Any small sharp object propelled with sufficient velocity	Vision often impaired. Intra-ocular tension low. Site of perforation may not be apparent. Usually prolapse of iris and disorganization of eye. May terminate in phthisis bulbi or sympathetic ophthalmia (p. 1569)
Rupture of choroid	Blunt injury to eyeball	Crescentic white and hemorrhagic area. May be extensive and cause loss of vision
Traumatic conjunctivitis	From irritants in industry such as acid vapors, liquid or dust particles, aniline, tar and metal, wood or stone particles	Pain, irritation, tearing and photophobia
Traumatic iridocyclitis	Blunt injury to eyeball	Blood in anterior chamber. Low tension. May terminate in atrophy of eyeball after protracted low grade inflammation
Vitreous hemorrhage	Blunt injury to eyeball	Marked visual impairment. Black reflex with ophthalmoscope. Fundus details obscured
Wounds of lids and conjunctiva	Local injury	Laceration

time he may employ non-operative therapy such as foreign protein injection (p. 1552), the administration of large doses of salicylates and body

baths of ultraviolet ray (p 1550) During this waiting period it is his responsibility to explain the situation to patient and next of kin so that all may have assurance when the final decision has been reached that the best of human judgment has been exercised

FOREIGN BODIES

Foreign bodies may enter the conjunctival sac or penetrate the cornea Injury to deeper structures carries the threat of sympathetic ophthalmia

In the Conjunctiva —*Nonmetallic foreign bodies* that lie free in the conjunctival sac are removed with a moist applicator A few drops of a local anesthetic solution are instilled the lid is everted and the irritant is lifted off with care to avoid a scratch of the cornea

Penetration of the conjunctiva by *metallic objects* or *burned ashes* requires reference to the specialist who may be required to accomplish removal with a *spud* (p 1555) or any sharp instrument

Conjunctivitis nodosa results when the irritating hairs of caterpillars or plants become lodged in the conjunctival sac After removal frequent irrigations with saline solution are required

Corneal Foreign Bodies —Corneal foreign bodies require immediate removal The resultant abrasion is best protected by instillations of castor oil and application of a protective dressing Penetration of the cornea places the uveal tract in jeopardy with the additional hazard of a *sympathetic ophthalmia* (p 1569) Prophylactic anti infective therapy with sulfonamide and/or penicillin is advisable in the interim between injury and consultation with the ophthalmologist

BURNS

Eyelid conjunctiva and cornea may be exposed to burns by heat and chemicals Photoretinitis may follow injudicious exposure to brilliant sunlight the glare of snow klieg lights sources of ultraviolet radiation and the flashes that result from welding and arc lights

Heat Burns —Burns of eyelids conjunctiva and cornea may result from steam gas ashes hot powder metals acids alkalies lime and irritant chemicals The immediate result is destruction of tissue such as that seen with burns elsewhere on the body In the conjunctiva the affected spot appears grey or white and is surrounded by redness and swelling of non eschirotic membrane Corneal burns are associated with ulceration and necrosis

Treatment —Local anesthetization facilitates complete removal of foreign particles and residual chemicals This is particularly emphasized in lime burns since the offending substance may lodge under the upper lid and in the fornix with continuing trauma Burns that involve *lids* alone are relieved by local applications of castor oil and cold compresses of saline solution or iced milk With *conjunctival burns* the pupil is dilated with 2 per cent homatropine castor oil is instilled at frequent intervals cold compresses are applied and the lids are separated once daily using a glass rod anointed with petrolatum to prevent adhesions

Corneal burns are specialist province and are treated in the manner of conjunctival burns The eye must not be bandaged but is left open if the burn has resulted from exposure to lime or mustard gas Deep

corneal ulcerations may perforate and cause *panophthalmitis* (p 1571) with injury to the *uveal tract* and the hazard of *sympathetic ophthalmia* (p 1569)

The late treatment of conjunctival and corneal burns is concerned with the prevention and management of cicatricial deformities Healing may be followed by a *symblepharon entropion ectropion ankyloblepharon* and *lagophthalmos* (Table 107 p 569) Healing of the corneal ulcer may result in opacification with disturbances in vision Management of these *late sequels is specialist province*

Photoretinitis —Exposure to excessive sunlight the glare of snow kleig and ultraviolet lights the flash of arc welding and the like may produce *conjunctivitis keratitis photoretinitis impairment of vision* or *central scotoma* These lesions are prevented by wearing tinted glasses (p 1538) or goggles and by the use of shields around the source of the ray After injury the patient requires isolation in a darkened room and application of cold compresses

DISPLACEMENT OF THE LENS

Dislocation or *luxation* of the lens and partial dislocation or subluxation may be congenital or acquired The disturbances are associated with defects in the suspensory ligament resulting from atrophy rupture stretching or imperfect development

The *congenital type* is generally partial tending to become complete in after years It is generally bilateral symmetrical and hereditary it may be associated with *arachnodactyly* (Marfan s disease) *Acquired dislocations* of the lens are traumatic or spontaneous In the traumatic type a direct blow upon the eye is the usual cause In spontaneous dislocation while the exciting cause may appear to be insignificant a defect in the zonule may result in lens displacement Ocular conditions which predispose to dislocation include *high myopia fluid vitreous choroiditis detachment of the retina* and *hypermature cataract*

Clinical Manifestations —*The clinical manifestations that suggest dislocation of the lens include visual disturbances impairment of accommodation changes in the refractive power* of the eye and *monocular diplopia* Partial dislocation or subluxation may be of minimal degree and may only be diagnosed *by the observation of a tremulous condition of the iris (iridodonesis)* Unequal depth of the anterior chamber may be noticed If subluxation is marked the border of the lens is visible in the pupillary area Complete dislocation may result in displacement of the lens anteriorly into aqueous or posteriorly into vitreous

Treatment —The treatment of lens dislocations lies in the hands of the specialist In partial dislocation it may be necessary only to prescribe proper glasses If the lens is dislocated into the anterior chamber the resulting inflammation with acute secondary glaucoma may require removal of the lens (p 1558) Dislocation into vitreous is ultimately more serious as removal of the lens then is technically more difficult

DETACHMENT OF THE RETINA

Detachment of the retina is a serious and not uncommon condition A hole or a tear in the retina resulting from retinal disease or injury is the main factor in the production and persistence of the detachment

Most detachments occur in people from fifty to sixty years of age and about two thirds are in myopes They generally occur after trauma often of minimal degree in persons predisposed because of senility and myopia Other causes include exudative chorioretinitis long standing iridocyclitis hypertensive retinopathies eclampsia and choroidal tumors and hemorrhages

DIFFERENTIAL DIAGNOSIS OF

Photophobia

Photophobia is usually accompanied by blepharospasm and may be caused by local and systemic disturbances

	DIAGNOSTIC FEATURES
Functional	Fatigue asthenopia neuroses and hysteria Order refraction (p 1537)
Adnexal	Foreign bodies local injuries physical and mechanical lesions of lids and conjunctivae Blepharitis Conjunctivitis Analogues of dermatoses Herpes ophthalmicus Make local examination with oblique illumination (p 3622) Identify pathogen by stains of exudat and epithelial scrapings (p 1546)
Lesions of Fibrous Tunic	Keratitis scleritis episcleritis or corneal ulcer Refer to specialist for slit lamp examination and epithelial scrapings (p 1546)
Lesions of Vascular Tunic	Iritis iridocyclitis or sympathetic ophthalmia Refer to specialist for examination by slit lamp and ophthalmoscope (p 1545)
Lesions of Neural Elements	Retinitis and retinitis pigmentosa Refer to specialist for fundus examination
Disturbances of Intra ocular Tension	Glaucoma with pain in eye elevation of tension and relief from miotics Avoid mydriatics
Systemic Infections	Upper respiratory infection with nasopharyngitis Measles with characteristic exanthem Pertussis with paroxysmal cough and lymphocytosis Meningitis and encephalitis with organic neurologic findings and changes in cerebrospinal fluid Variola varicella and rubeola with characteristic rashes (p 172) Poliomyelitis with evidences of anterior horn involvement (p 457)
Metabolic Disturbances and Poisonings	Migraine and epilepsy Allergic conjunctivitis and rhinitis with eosinophilia Vitamin A deficiency with night blindness (p 1535) Cinchonism (p 862)
Neurogenic	Facial and trigeminal neuralgias (p 1484)

Clinical Manifestations—In retinal detachment the patient first may notice *spots or a cloud before the eyes* and *flashes of light* (*photopsia*) If detachment involves the macula central vision is impaired

Ophthalmoscopy—Ophthalmoscopic examination usually reveals a fluid vitreous containing numerous filmy floating opacities The retina is thrown into folds appears considerably paler than normal and finally assumes a

greyish tint The detached retina is brought into focus with much stronger plus lenses than the remainder of the retina *The retinal vessels appear* black in contrast to the red vessels seen elsewhere they seem small and lose their central reflex The *retinal tear* usually is situated toward the per iphery and appears as a bright red spot The color is due to choroid shin ing through the hole Successful operative treatment depends on the accurate localization of the tear

Course and Treatment—The great majority of *untreated retinal detach ments* terminate in complete detachment degeneration of the eye and blindness Spontaneous reattachment rarely occurs

DIFFERENTIAL DIAGNOSIS OF

Exophthalmos (Proptosis)

Bulging of the eyeball may be unilateral or bilateral In either instance the etiologic factor may be local or systemic

	DIAGNOSTIC FEATURES
Ophthalmic	Edema inflammation or neoplasm of orbit with visible and palpable changes (p 1615) Cav ernous sinus thrombosis with fever and bac teremia (p 1447) High myopia with fundus changes and refractive error (p 1536) Vari cosities of orbit with increased bulging when head is lowered.
Lesions of Contiguous Structures	Hydrocephalus with pumpkin head. Sup purative spheno-ethmoiditis with radiographic changes and demonstrable pus
Metabolic	Hyperthyroidism with elevation of B M R and therapeutic response to iodide Hutchinson s tumor of the adrenals in infancy Schuller Hand Christian disease with diabetes insipidus and cholesterol deposits in subcutaneous tis sues and bones Poisoning with potassium cyanide
Systemic Infection	Epidemic encephalitis with neurologic find ings and changes in cerebrospinal fluid (p 441)
Vascular	Arteriovenous aneurysm of internal parotid and cavernous sinus with pulsating exoph thalmos

Operative treatment (p 1558) represents a great advance in opthal mology and produces a satisfactory result in more than 60 per cent of patients Reoperation greatly increases favorable results With associated pre existent inflammation of retinopathy surgery is contraindicated

EXOPHTHALMOS (PROPTOSIS)

Exophthalmos is an undue protrusion of eye from orbit as measured by the exophthalmometer (p 1546) The condition most often results from the presence of *hyperthyroidism*

Clinical Manifestations —Marked exophthalmos causes *impaired motility* of the eyeball *diplopia* and *lagophthalmos* (p 1569) The latter may result in exposure of cornea and keratitis with ultimate loss of the eye if untreated Involvement of the optic nerve leads to impairment of vision and the presence of a neuritis

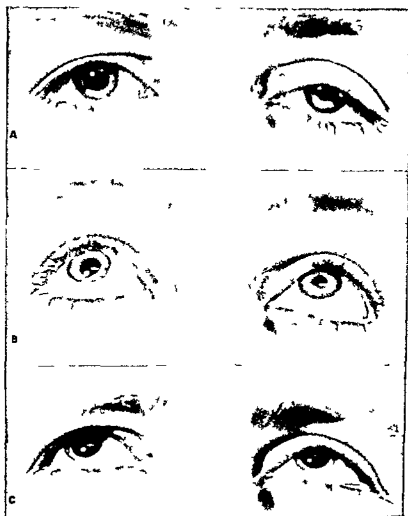


Fig 306 —*A* Paralysis of the left sympathetic nerve Note the small palpebral fissure, the lowering of the upper eyelid (pseudoptosis) and small pupil also the slight enophthalmos *B* Picture taken one hour after several drops of 4 per cent cocaine had been instilled The pupil did not dilate and the palpebral fissure remained the same *C* Shows the effect of homatropine instilled in each eye Both pupils well dilated in twenty minutes

Treatment —Treatment is directed at the underlying cause The practitioner should warn the hyperthyroid patient that there may be little regression of the exophthalmos following iodine and deracil therapy or thyroidectomy (p 1214) In the presence of lagophthalmos plastic surgery of the lid may be required More formidable procedures include re-

* Casten in Berens The Eye and Its Diseases

moval of orbital fat ganglionectomy and the Naffziger operation upon the orbit

In hyperpituitary exophthalmos thyroidectomy may markedly aggravate the exophthalmos in such instances thyroid extract or iodine may be helpful plastic surgery of the lids is contraindicated and decompression of the orbit may be urgently required

PULSATING EXOPHTHALMOS

In pulsating exophthalmos a *bruit* is audible when the stethoscope is placed over eye or forehead The patient complains of head noises and local pain the observer notes marked dilatation of the vessels of the retina conjunctiva and lids Vision may be impaired and an optic neuritis may develop Not infrequently there are associated paralyses of third and sixth cranial nerves (p 1645 1647)

Compression of the internal carotid artery causes pulsations and bruit to diminish or disappear since the causative mechanism is usually an *arteriovenous aneurysm* involving internal carotid artery and cavernous sinus The condition may be relieved by gradual compression of the carotid first on one side and then if necessary on the other There is no necessity to institute therapy unless for cosmetic reasons in which case plastic surgery is recommended

ENOPHTHALMOS

Enophthalmos is rare It occurs with decrease in the amount of orbital fat with dehydration such as that occurring in cholera following paralysis of the upper sympathetic chain (Horner s syndrome) following injury to the margin of the orbit and after operations on the recti

PAPILLEDEMA

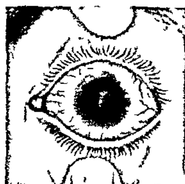
Pathogenesis —Pathologically papilledema is a simple swelling of the optic nerve head due to edema of the individual nerve fibers The accompanying venous congestion superimposes a metabolic disturbance which interferes with the normal flow of tissue fluid

Clinical Manifestations —Papilledema is not necessarily associated with derangement of visual acuity Only when the condition has been present for a considerable period of time does diminution of vision occur When using the ophthalmoscope the changes first noted are *increased redness of the disk* with slight *haziness and blurring of the upper and lower margins* especially on the nasal side There may be some *fullness of the veins* the surrounding retina shows greyish white striations as evidence of edema

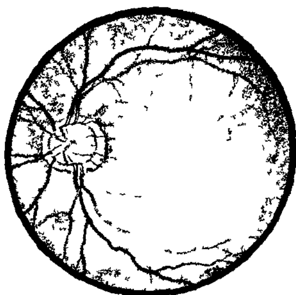
Once established the ophthalmoscopic appearance of papilledema is very marked There is considerable swelling of the disk with obvious blurring of the margin so that it is difficult to demarcate the nerve head from the edematous retina Sometimes only the confluence of the larger vessels indicates the position of the disk hemorrhages and exudates appear the veins become enormously distended and tortuous while the arteries remain small

The *amount of elevation* of the nerve head is measured by the specialist who notes the strongest plus lens with which he can see the vessels of the disk as compared to the strongest plus lens with which he can see

is grayish in color and there is *cupping* or *excavation* involving the central area with a peripheral overhanging edge Cupping is due to increased tension and may be appreciated by following the course of the *central retinal vessels* they are pushed toward the nasal side and climb over the sharp overhanging rim with an acute bend when tension is very high *arterial pulsations* may occur Cupping does not occur until glaucoma has been well established over a period of years



A



B

Fig 808—*A* Acute glaucoma *B* Cupping of the disk in chronic glaucoma

Flevation of Intra ocular Tension—The important diagnostic findi in simple glaucoma is *elevated intra ocular tension* which is present fro the onset although it may become higher during the course of the disea This may be ascertained by palpation of the eye with the fingers Th test should be performed by practitioners whenever the slightest su picion of glaucoma exists If it appears that an increased tension is pre

* Gifford Textbook of Ophthalmology

ent the patient is sent to the specialist for *tonometric examination* (p 1545)

Course—Chronic simple glaucoma if unarrested eventually goes on to complete blindness

Treatment—The treatment of simple glaucoma belongs in the hands of the specialist who controls the tension by the use of *miotics* (p 105) The patient is observed periodically and special attention is directed to visual acuity and fields and intra-ocular tension If the condition progresses one of the type of drainage operations is advised (p 1558) The most usual procedure is the *Elliot trephine* operation (p 1558)

Congestive Glaucoma—Congestive glaucoma may be acute or chronic Acute congestive glaucoma may become superimposed upon simple glaucoma or it may appear without warning and with great suddenness in an eye that is apparently healthy It is usually preceded by mild *prodromal* attacks with diminution in acuity of vision fogginess and the appearance of a ring of rainbow tints around foci of light

Clinical Manifestations—In acute congestive glaucoma the patient is generally awakened by excruciating pain in the eye profuse *lacrimation* and intense *trigeminal neuralgia* He notes rapid *failure of vision* which may progress to loss of light perception within a few hours The local symptoms are associated with *nausea* and *vomiting* evidences of shock or flushing and a slight pyrexia

Intra ocular tension is markedly increased as revealed by comparing the palpatory sensations in the affected as against the nonaffected eye The involved eye is intensely red and congested The lids are edematous the conjunctiva chemotic the globe tender and the cornea is dull and steamy The pupil is widely dilated vertically oval in shape and unresponsive to light (p 1533) Ophthalmoscopic examination is difficult because of edema of the cornea and if the optic disk can be seen it is edematous and hyperemic

Course—Following the acute phase the eye may seem normal but actually it has progressed to the stage of *chronic congestive glaucoma* The symptoms and signs persist to a varying degree exacerbations of acute glaucoma are encountered and the final stage is that of *absolute glaucoma* resulting in a blinded hard and painful eye

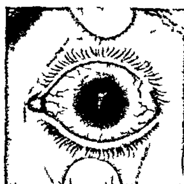
Treatment—In the acute phases cold compresses are applied and *opiates* are given in large doses A combination of 2 per cent *pilocarpine* and 0.5 per cent *eserine* is instilled into the eye every ten or fifteen minutes for 6 doses and then every two hours to effect complete miosis and reduction of intra ocular tension Meanwhile the specialist is consulted Within a few hours the miotics may result in a dramatic subsidence of symptoms and serve as a therapeutic test If relief is not obtained the ophthalmologist employs instillations of 0 1 to 0 2 diisopropyl fluorophosphate

The operation of choice is an *iridectomy* (p 1558) which should be performed even if the tension is reduced to normal A successful iridectomy usually results in permanent and complete relief of acute congestive glaucoma Less satisfactory results are observed in chronic simple glaucoma

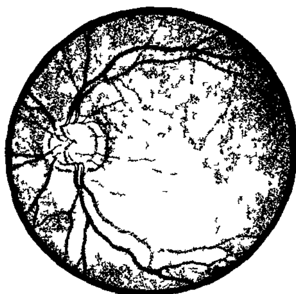
SECONDARY GLAUCOMA

In secondary glaucoma a recognized pathologic lesion of the eye is complicated by increase in intra ocular pressure As the basic condition

is grayish in color and there is *cupping* or *excavation* involving the central area with a peripheral overhanging edge Cupping is due to increased tension and may be appreciated by following the course of the *central retinal vessels* they are pushed toward the nasal side and climb over the sharp overhanging rim with an acute bend when tension is very high *arterial pulsations* may occur Cupping does not occur until glaucoma has been well established over a period of years



A



B

Fig 308 —*A* Acute glaucoma *B* Cupping of the disk in chronic glaucoma

Elevation of Intra ocular Tension—The important diagnostic finding *in simple glaucoma* is *elevated intra ocular tension* which is present from the onset although it may become higher during the course of the disease This may be ascertained by palpation of the eye with the fingers This test should be performed by practitioners whenever the slightest suspicion of glaucoma exists If it appears that an increased tension is pres

Etiology and Clinical Manifestations.—The common basic lesions in secondary glaucoma include intra-ocular inflammation, trauma, changes in the lens, vascular anomalies of the retina, intra-ocular tumors, detachment of the retina, intra-ocular hemorrhage, atrophic and sclerotic conditions of the eye, venous obstruction in the orbit, and congenital anomalies. The clinical manifestations are those of increased intra-ocular tension (p. 1526) superimposed on the more fundamental lesion.

Treatment.—The treatment of secondary glaucoma depends on the nature of the underlying condition. If control is possible, the glaucoma may disappear. Otherwise *iridectomy* (p. 1558) or the Lagrange operation (p. 1558) is indicated.

EPIDEMIC DROPSY

The condition which is seen in India and is known as *epidemic dropsy* is characterized by glaucoma (p. 1578), general edema, hypertrophy of the heart, and a peripheral neuritis suggesting a thiamine deficiency (p. 616). Medicinal treatment is of no avail, and interestingly enough only operation is of help.

OCULAR HYPOTENSION

Ocular hypotension or *ophthalmomalacia* occurs in a number of conditions such as myopia, retinal detachment, trauma, infections and inflammations of the eye. Hypotension may occur in severe general illnesses, particularly poisonings by *quinine* or *barbiturates*, in *diabetic coma*, and in primary anemias.

Although the clinical symptoms of hypotony are by no means striking, grave visual disability may appear and persist. The *treatment* of this condition requires attention to the elimination or correction of the more basic abnormality.

DIFFERENTIAL DIAGNOSIS OF

Pain in the Eye

The complaint of pain in the eye requires intensive investigation At times the cause may be as simple as a cinder located in the conjunctival sac but again the disturbing circum tances may be a mechanism as serious as acute glaucoma

	DIAGNOSTIC FEATURES
Functional	Ametropia pre byopia asthenopia or pasm of accommodation Correct refractive error (p 1536)
Psychogenic	Malingering and hysteria Normal findings on examination
Neurogenic	Trigeminal neuralgias
Adnexal	Physical chemical and mechanical injuries to the eye Foreign body Exposure to tear-gas Hordeolum chalazion dacryocystitis or con junctivitis Examine by oblique illumination and inversion of lid (p 3622) Make cultures and smears from exudate and epithelial scrapings (p 1546) Look for analogues of the der matoses particularly herpes ophthalmicus with characteristic vesicle (p 1629)
D sturbances of Fibrous Tunic	Keratitis episcleritis scleritis and corneal ulcer Refer to peciali t for slit lamp examina tion and for microscopy of epithelial scrapings (p 1546)
Disturbances of Vascular Tunic	Choroiditis iridocyclitis sympathetic oph thalmia Refer to specialist for slit lamp and fundus examinations (p 1545)
Disturbances of Neural Elements	Retinitis photoretinitis and obstructions of retinal arteries or veins Cavernous sinus thrombosis Refer to pecialist for fundus ex amination (p 1545)
Disturbances of Intra ocular Tension	Glaucoma with hard eyeball and relief from use of miotics Avoid mydriatics
Orbital	Orbital cellulitis periostitis and osteomyelitis Get x rays of skull and nasal accessory sinuses Consult rhinologist and ophthalmologist
Contiguous Infections	Particularly acute inflammations of nasal accessory sinuses Get x rays and consult rhinologist for local examination and lavage of sphenoids
Systemic Infections	Upper respiratory infection with nasopharyn gitis Measles with cutaneous eruption Dengue in epidemic areas Influenza with respiratory manifestations and myalgias Men ingococcemia with bacteremia and general ized eruption
Metabolic	Particularly migraine and epilepsy

has usually brought the patient to the specialist and the glaucoma gener ally develops during treatment the problem is not so urgent a concern of the practitioner as are the primary varieties

General Paresis (p 1377)
Argyll Robertson pupil Ocular palsy Optic neuritis and atrophy

Hepato lenticular Degeneration (p 1418 1977)
Kayser Fleischer ring of greenish brown pigmentation in deep layers of cornea

Hysteria (p 1353)
Impairment of vision amaurosis perversions of color vision micropsia macropsia nyctalopia diplopia monocular diplopia anesthetic cor nea photophobia disturbances of intra and extra ocular muscles and tubular field defects (gun barrel)

Increased Intracranial Pressure (p 1421)
Papilledema

Meningitis (p 1462)
Oculomotor paralysis Optic neuritis

Mongolian Idiocy (p 2774)
Slit eyes and lenticular opacities

Multiple Sclerosis (p 1504)
Retrobulbar neuritis central scotoma nystagmus transient oculomotor paralyses and temporal pallor of disk

Myasthenia Gravis (p 2886)
Ptosis oculomotor paralyses diplopia and impaired convergence and accommodation

Myotonia Atrophica (p 2888)
Cataract

Myotonia Congenita (p 2886)
Cataract

Optic Pathway Lesion (p 1645)
Homonymous hemianopsia

Occipital Lobe Lesion (p 1426)
Localized field defects or perceptual blindness and papilledema

Pressure on Optic Nerve (p 1645)
Blindness loss of pupillary reflex and scotomas

Quadrigeminal Plate Lesion (p 1426)
Paralysis of upward gaze diplopia Argyll Robertson pupils and papilledema

Red Nucleus Lesion (p 1496)
Bilateral papilledema with homolateral oculomotor paralysis

Schilder s Disease (p 1640)
Optic neuritis and bilateral atrophy

Tabes Dorsalis (p 1464)
As general paresis

CHAPTER 78

OPHTHALMIC MANIFESTATIONS OF NEUROMUSCULAR, CARDIOVASCULAR AND HEMATOPOIETIC DISORDERS

LOCAL ocular manifestations are frequently encountered in disturbances of the neuromuscular cardiovascular and hematopoietic systems These phenomena are easily visible herald signs of profound afflictions which other wise may be unsuspected The recognition of the causal association has therapeutic as well as diagnostic significance since indication is afforded for a plan of treatment of wider scope than mere local or symptomatic measures

OPHTHALMIC MANIFESTATIONS OF NEUROMUSCULAR DISORDERS

Because of the clarity with which the optic nerves may be viewed by ophthalmoscopy neurologic disturbances are often first recognized by the manifestations which are here encountered Other aids to neurologic diag nosis are afforded by disturbances of the visual field and of the extra ocular muscles that are innervated by the cranial nerves

Amaurotic Family Idiocy (p 1584)
Optic atrophy with cherry red spot at macula

Central Chiasm Lesion (p 1645)
Bitemporal hemianopsia and optic atrophy

Cerebellar Lesion (p 1426)
Bilateral papilledema Bilateral partial oculomotor paralysis

Cerebellopontine Angle Lesion (p 1426)
Bilateral papilledema Homolateral anesthesia of cornea Homolateral abducens paralyses and nystagmus

Chorea (p 191)
Blepharospasm

Encephalitis (p 441)
Ocular palsies and the syndrome of paralysis agitans

Epilepsy and Migraine (p 1506 1515)
Scintillating scotomas and ophthalmoplegia

Friedreich s Ataxia (p 1415)
Pseudonystagmus

Frontal Lobe Tumor (p 1425)
Foster Kennedy syndrome of ipsilateral optic atrophy and contra lateral papilledema

Cerebral Aneurysms (p 968)
Oculomotor paralyses

Malignant Hypertension
Arteriosclerotic changes plus papilledema Venous engorgement retinal edema and retinal detachment and cotton wool exudates Radiating star figures at macula Flame shaped hemorrhages

Pulmonary Stenosis (p 971)
Congestion tortuosity and cyanosis of retinal vessels

Raynaud s Disease (p 1000)
Spasm of retinal vessels

Subacute Bacterial Endocarditis (p 1071)
Conjunctival and retinal petechiae Superficial retinal hemorrhages Embolization of central artery

Thrombo angiitis Obliterans (p 1020)
Vessels appear as white strands due to peri and endovasculitis

Thrombosis of Cavernous Sinus
Immobility of eye with increasing exophthalmos Distention of retinal veins papilledema and optic neuritis Edema over mastoid

Varicose Veins of Orbit
Intermittent exophthalmos which lessens when head is held erect and increases when head is depressed

OBSTRUCTION OF THE CENTRAL RETINAL ARTERY

Obstruction of the central retinal artery may be due to spasm or organic closure Spastic occlusion occurs with systemic evidences of vasomotor instability particularly in migraine allergy and hypertension Organic blockage is most often due to arterial thrombosis associated with a generalized endarteritis but it may also follow embolism in cardiac disease or subacute bacterial endocarditis

Clinical Manifestations—*Obstruction of the central retinal artery is an* ophthalmic emergency in which the patient becomes suddenly and almost completely blinded The left eye is more generally affected in an embolization and the affliction is characterized by the fact that it is not accompanied by pain When the main vessel is occluded blindness is complete even to the perception of light If a branch is blocked there may be only a sector shaped defect of the visual field

Ophthalmoscopy—The ophthalmoscopic picture of complete closure of the central retinal artery is very characteristic The abnormally pale nerve head is obscured by edema The arteries are thinned and can be followed for only a short distance from the disk The veins are also narrowed and the blood column may be broken up into segments giving a beaded or fragmented appearance In a short time the retina loses its transparency and becomes pale edematous and milky Later at the macula a bright cherry red spot is observed where the red reflex of the choroid shines through the thin fovea standing out in marked contrast to the neighboring whitish retina If a collateral cilioretinal artery is present an island of

Temporal Lobe Lesion (p 1426)
Papilledema and hemianopic field defect

Trigeminal Neuralgia (p 1482)
Pain in eye

OPHTHALMIC MANIFESTATIONS OF CARDIOVASCULAR DISEASE

The ophthalmic manifestations of cardiovascular disease for the most part are local manifestations of a systemic disturbance Only in rare instances such as obstruction of the central retinal artery or veins is the clinical condition a predominantly isolated affliction

Acute Glomerulonephritis
See Hypertensive Retinopathy p 2373

Aortic Aneurysm (p 1026)
Mydriasis and widening of palpebral fissure

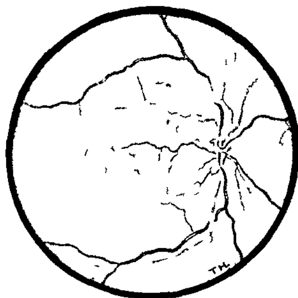


Fig 309 —Arteriosclerotic retinopathy

Aortic Insufficiency (p 970)
Arterial pulsations of retinal artery due to high pulse pressure

Arteriosclerosis
Increased translucency of arteries (copper wire and silver wire) Beading tortuosity and attenuation of arteries and sheathing of vessels due to fibrous perivasculitis Constriction of veins (Gunn s sign) at arteriovenous crossing Irregularity of vascular lumen Thrombosis of central artery or vein Hemorrhages and exudates

Arteriovenous Aneurysm of Internal Carotid and Cavernous Sinus
Pulsating exophthalmos (p 1577) with bruit Dilatation of vessels of retina conjunctiva and lids Optic neuritis Pulsation lessened by compression of internal carotid

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Treatment.—Whatever the cause of [illegible] artery prompt treatment may save [illegible] by inhalations of amyl nitrite [illegible] dermic injection of acetylcholine or [illegible] or aminophyllin. The globe may be massaged and [illegible] dilate a paracentesis in order to lower intraocular pressure. In [illegible] of the various forms of therapy [illegible] improvement may occur. Nevertheless [illegible] too great reliance upon the healing [illegible] of knowing which of the [illegible] may be permanent.

OBSTRUCTION OF THE RETINAL VEINS

Obstruction of the retinal vein or one of its branches is more common than closure of an artery. Whereas in the occlusion of an artery the worst complication is blindness in that eye, closure of the central retinal



Fig 311 —Pernicious anemia

vein may be associated with *secondary glaucoma* (p 1581) and terrific pain amenable to no therapy save removal of the eye. The condition usually occurs in older people when it is associated with arteriosclerosis, slowing of the blood flow and endophlebitis. In young people it may follow febrile diseases such as influenza.

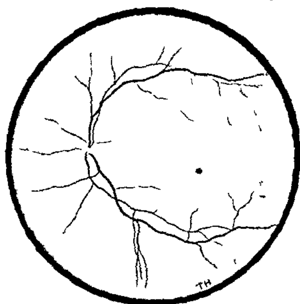
Clinical Manifestations.—At the time of the accident the symptoms are confined to *loss of vision*. In complete thrombosis loss of sight comes on rapidly but not with the dramatic suddenness and completeness of arterial obstruction. In thrombosis of one of the branches of the central retinal veins the loss of vision is limited to the area served by the occluded branch.

Ophthalmoscopy.—When the trunk of the central vein is blocked the ophthalmoscopic picture is very striking: the nerve head is completely obscured by edema and numerous *linear hemorrhages* are arranged radially. *Scattered throughout the rest of the fundus are other hemorrhages*

Courtesy of Dr Arthur Bedell

relatively normal retina may remain in the central area with preservation of central vision

If obstruction of the artery is not overcome the retina atrophies after a few days and later there is optic atrophy The end picture is character



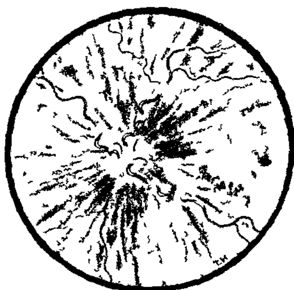


Fig 310—*A* Closure of central retinal artery *B* Thrombosis of central retinal vein

ized by the appearance of thin shrunken arteries represented by white lines atrophy of the nerve fibers and the ganglion cell layers of the retina with preservation of the outer retinal layers

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CHAPTER 79

OPHTHALMIC DISTURBANCES IN METABOLIC DISORDERS AND POISONINGS

METABOLIC disorders and poisonings may be reflected in the visual apparatus by a variety of manifestations The most frequent of these is the cataract later described in detail (p 1592) The less common are tabulated in Table 109

TABLE 109 —OPHTHALMIC MANIFESTATIONS OF METABOLIC DISORDERS AND POISONINGS

Lesion	Site	Associated Condition
Pinguecula	Yellow triangular patches situated in bulbar conjunctiva on either side of cornea	Following exposure and in senility Brown pinguecula in Gaucher s disease (p 1133)
Xerosis	Of the conjunctiva	With burns trachoma or vitamin A deficiency
Pigmentation	Of sclera	Ecchymos s following subconjunctival hemorrhage Yellow tint in icterus and carotinemia Black p gmentat on in Addison s disease and ochronosis Blue sclerotics in fragil tas oss um S lver deposits in argyrosis Kayser Fleischer ring in hepatolent cular degeneration (pp 1418 19)
Arcus sen l (gerontoxon)	Opaqu greyish white rin just with n corneal margin	Famil al In a ter osclerosis
Embryotoxon	At ma g n of cornea cont nuous with scl ra	Congenital anomaly
Keratomalacia	Of orn a	In vitamin A deficien y
Dystroph es	I ne opac t es and va uoles in endo th l um an l ep thel um of cornea	May be fam l al an l hereditary o r lated to rterio clero is
D r n (collo d) bod es	Of cl oro d appearing as hyal ne ex cres en e of lam na v t ea	Degenerative pl nomena
Ang o l st eaks	R d l sh la k b own lin s of choro d situated a ound the d sk	W th p eud xantl oma elasticum
Macular degene a t on	Small l emo rhag s of r tina fol lowed by p gm ntary or cystic l ang s May produce hole in macula w th the appearance of a deep-re l punched-out area	Usually senile

of various types and sizes The fundus picture is dominated by the enormously distended and *tortuous retinal veins* which may be several times their normal size The arteries are narrowed

In a branch thrombosis the pathology is limited to the area supplied by the tributary veins The condition is readily diagnosed by the enormous dilatation of the *occluded branch as compared to other uninvolved* branches Perhaps even more characteristic are the numerous hemorrhages which radiate out from the nerve head forming a triangle with apex adjacent to nerve head

Treatment —*Heparinization* (p 1050) by the Loewe method or the oral use of dicoumarin (p 1050) should be undertaken without even waiting the arrival of the consultant ophthalmologist The complication of secondary glaucoma impends in 10 to 20 per cent of instances when the central retinal vein is occluded In *branch thrombosis* glaucoma does not occur Needless to say mydriatics are contraindicated under any circumstances

OPHTHALMIC MANIFFSTATIONS OF HEMATOPOIETIC DISORDERS

Diseases of the blood and blood forming organs are prone to be reflected in the delicate tissues of the organs of vision The local manifestations include hemorrhage edema and thromboses

Anemia of Hemorrhage (p 1056)

Acute edema of optic nerve and retina may cause transient blindness

Hyperchromic Anemia (p 1077)

Pallor of nerve narrow and pale retinal arteries flame shaped superficial hemorrhages and cotton like exudates

Hypochromic Anemia (p 1089)

If severe may cause retinal hemorrhages and optic neuritis Pale conjunctiva Pearly sclera

Leukemias (p 1100)

May be associated with edema of disk exudates in retina and white centered hemorrhages

Polycythemia (p 1092)

May result in distention and engorgement of veins purple color to retina and congestion of conjunctiva

Purpuras (p 1121)

May cause subconjunctival retinal hemorrhages edema and neuritis of optic nerve

Hemophilia (p 1118)

May produce hyphemia and hemorrhages of retina and orbit

no clinical significance and complete cataracts involve almost the whole lens

If vision is impaired to any significant extent *treatment* is in the hands of the specialist who usually performs a *discission* (p 1558) The retina and macula often do not develop perfectly in the presence of congenital cataract and even after an eminently successful operation vision may be considerably impaired

Degenerative Cataract —The *senile* degenerative cataract is the most frequent clinical type It is quite common after the fiftieth year although sometimes it is seen as early as forty Both eyes usually are involved but



Fig 312 —Arcus senilis



Fig 313 —Cholesterol bodies in the vitreous (synchysis scintillans)



Fig 314 —Mature senile cataract

generally one is more affected than the other The development of the cataract is variable growth may be slow or rapid In the incipient stage of a senile cataract the opacity is usually characterized by streaklike spots As the lens absorbs fluid and swells the cataract enters the *immature stage* When the lens loses most of its fluid and shrinks it enters the *mature stage* and becomes opaque and of a dull grey or amber color The stage of *hypermaturity* may be associated with dislocation of the lens and degenerative changes that terminate in loss of the eye

Pathologic Cataract —The pathological cataract may be associated with a variety of local and systemic disturbances such as osmotic changes in

TABLE 109 —OPHTHALMIC MANIFESTATIONS OF METABOLIC DISORDERS AND POISONINGS (*Continued*)

Lesion	Site	Associated Condition
Retinitis pigmentosa	A hereditary chronic and bilateral process beginning in childhood and terminating in blindness by middle life A degeneration of retinal neuro-epithelium particularly of the rods Results in night blindness increasing contraction of peripheral fields with eventual impairment of central vision Ophthalmoscopy reveals attenuation of retinal vessels pigmentary deposits and a yellow waxy appearance of the atrophic disk	Of unknown origin but may be complicated by cataract and glaucoma.
Macular and lipoid degeneration	Of retina	In amaurotic family idiocy lipoid histiocytosis (Niemann Pick) and Laurence-Moon Biedl syndrome
Dust like haziness	Of vitreous	In cyclitis and choroiditis
Asteroid bodies	Snow ball opacity in vitreous	In advanced age
Synchysis scintillans	Showers of moving silvery and golden particles of cholesterol in degenerated and fluid vitreous	Of unknown etiology
Muscae volitantes	Subjective spots before the eyes"	With errors of refraction especially myopia In fatigue and "auto-intoxication"

CATARACT

The cataract is an opacity of the lens or its capsule It is not necessarily associated with significant decrease in vision

Etiology —The lens carries on an active metabolism The most important features in the development of cataract are diminished lens metabolism decrease in lens permeability and loss of substances active in oxidation such as cysteine glutathione and ascorbic acid Experimental cataracts have been produced by mechanical injuries physicochemical causes irradiation decreased permeability of the capsule interference with nutrient supplies anoxemia lack of sufficient proteins tryptophan or cysteine toxic effects of naphthalene lactose galactose thallium and dinitrophenols and parathyroidectomy

In man cataract is primarily associated with senility Factors that may participate in its development include heredity interference with the local nutrient supply of the lens general metabolic disturbances vitamin deficiency and an attack of rubella (p 417) in the first trimester of pregnancy

Developmental Cataract —Developmental cataracts are lenticular opacities due to aberrations in the normal development of lens fibers and epithelium The polar cataract is a small central opacity which may or may not reduce vision to a significant extent Central cataracts occur near the sutures or in the fetal nucleus Punctate cataracts are generally of

fection are eliminated or drained Metabolic errors such as *uncontrolled* diabetes mellitus are remedied and hypertension is reduced if possible

In general it is better to avoid operation if vision is good in one eye The strong correction required after cataract extraction results in a 30 per cent enlargement of the image Glasses are poorly tolerated due to inability to fuse the larger image of the operated eye with that of the unoperated eye The surgical procedures performed for cataract are described elsewhere (p 1558) *Discissions* (p 1558) are advised in *congenital* and traumatic cataracts in patients below the age of thirty years *Intracapsular* or *extracapsular cataract extractions* are indicated in senile degenerative varieties An *iridectomy* (p 1588) may be wise as a preliminary to extraction in hypertensives and diabetics Secondary cataracts are managed by discission

LOCAL MANIFESTATIONS OF SYSTEMIC METABOLIC CONDITIONS

Metabolic disturbances of the organs of vision may be local manifestations of poisonings with drugs or chemicals or the effects of widespread metabolic abnormalities

OPHTHALMIC MANIFESTATIONS OF SYSTEMIC POISONINGS WITH DRUGS AND CHEMICALS

Acute Alcoholism (p 3848)
May be associated with incoordination of pupil impaired reaction to light or temporary amaurosis

Chronic Alcoholism (p 3851)
May cause toxic amblyopia or central scotoma May be avitaminosis (p 3266)

Methyl Alcohol (p 756)
May result in complete blindness with pupils dilated optic neuritis retinal hemorrhages and optic atrophy

Aniline (p 756)
May produce dark red fundus constriction of retinal vessels hemorrhage central scotoma and peripheral contraction of visual fields

Aminopyrine (p 3833)
Urticaria of lids is observed as idiosyncrasy

Arsenic (p 116)
Toxic amblyopia occurs *especially with tryparsamide* (p 120) *May result in optic atrophy and concentric contraction of peripheral* fields of vision

Aspidium (p 1895)
Bilateral amaurosis and optic atrophy as idiosyncrasy

Atropine (p 3875)
Paralysis of accommodation and mydriasis may precipitate acute glaucoma (p 1578)

Carbon Monoxide (p 747)
Overdose results in mydriasis ptosis ophthalmoplegia and progressive loss of central vision

diabetes and cholera There may be for instance *endocrine cataracts* in parathyroid tetany and myxedema cataracts with myotonic dystrophy myotonia congenita and Mongolian idiocy *dermatogenous cataracts* in neurodermatitis scleroderma and poikiloderma atrophicans *toxic cataracts* from dinitrophenol paradichlorobenzene (used as an insecticide or moth repellant) and ergot and *cataracta cachectica* which occurs in acute toxic illnesses

Complicated Cataract—The complicated cataract follows various intra ocular diseases It is presumably due to derangement of the metabolism of the lens by the diffusion into it of toxins from intra ocular fluids The main and earliest changes are seen in the region of the posterior pole of the lens This type of cataract follows usually severe ocular disease including iridocyclitis retinal detachment absolute glaucoma and intra ocular tumor

Secondary Cataract—Secondary cataract occurs in the remnants of the lens left behind after extracapsular operation or destruction by traumatism

Clinical Manifestations—The most important symptom of cataract is *diminished visual acuity* The degree of involvement depends upon the situation and extent of the cataract being greatest when it is central and diffuse Vision is best in dim light when pupils are dilated

At the onset of cataract the patient may complain of *black spots* which occupy a fixed position in the visual field *Polyopia* occurring in one eye is another frequent early symptom in which the images of objects are distorted or reduplicated due to irregular refraction within the lens This change also causes halos and stars around lights Myopia often develops in the early stages of cataract due to increased refractive power of the lens This second sight may cause the presbyopic patient to discard reading glasses

The objective signs of cataract consist of opacities in the lens Examination by *oblique illumination* (p 3622) shows a greyish or whitish opacity on a black background With the ophthalmoscope using a zero lens *at a distance a black opacity is seen on a red field* If the cataract is more or less complete the entire pupil appears greyish and the fundus reflex is absent

The complications of cataract are few A secondary rise in intra ocular tension may be due to swelling of the lens If the cataract is not removed when it is ripe and is allowed to become hypermature (*morgagnian cataract*) the hard nucleus of the lens floats about in the liquefied cortex Operation at this stage is difficult and rarely successful Unoperated the hypermature cataract may become dislocated and the eye may degenerate

Treatment—Attempts to stay the progress of lenticular opacities are difficult to evaluate since the course of cataract is variable and many never go on to maturity The local use of *dionin* (p 1548) has survived several centuries probably for want of something better A *high vitamin diet* with accessory feedings of vitamin B complex (p 682) may be recommended *Desensitization with lens protein has been tried but* the changes in the lens seem irreversible Very often a careful *refraction* and prescription for glasses will produce sufficient vision to postpone operation

Surgery affords the only positive means of curing cataracts Operative interference is preceded by thorough systemic investigation Foci of in

fection are eliminated or drained Metabolic errors such as uncontrolled diabetes mellitus are remedied and hypertension is reduced if possible

In general it is better to avoid operation if vision is good in one eye The *strong correction required after cataract extraction results in a* 30 per cent enlargement of the image Glasses are poorly tolerated due to inability to fuse the larger image of the operated eye with that of the unoperated eye The surgical procedures performed for cataract are described elsewhere (p 1558) *Discissions* (p 1558) are advised in *congenital* and traumatic cataracts in patients below the age of thirty years *Intracapsular* or *extracapsular cataract extractions* are indicated in senile degenerative varieties An *iridectomy* (p 1558) may be wise as a preliminary to extraction in hypertensives and diabetics Secondary cataracts are managed by discission

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Carbon Disulfide (p 747)
May cause photophobia nystagmus punctate keratitis impaired accommodation, micropsia macropsia and monocular diplopia

Bromide (p 3838)
Conjunctivitis

Caffeine (p 3860)
Amblyopia

Cannabis Indica
May result in impaired accommodation mydriasis visual hallucinations and amblyopia

Chloral (p 3837)
Miosis and later mydriasis from overdose

Chloroform (p 3925)
Mydriasis in profound poisoning

Chrysarobin (p 3118)
May cause bilateral conjunctivitis and keratitis

Cocainism (p 3916)
Visual hallucinations micropsia diplopia and amblyopia may follow

Digitalis (p 860)
Perversion of color sense

Dinitrophenol (p 754)
Cataract formation may result from obesity cures

Ergotism (p 240)
Spasm of retinal vessels pallor of optic disk neuroretinitis and cataract formation may result from overdosage or idiosyncrasy

Ether (p 3925)
Mydriasis from deep poisoning

Lead (p 762)
May cause extra ocular paralyses papilledema optic neuritis and hypertensive neuroretinitis

Mercury (p 765)
Retinal degeneration and hemorrhages may be produced

Methylene Blue
Greenish blue fundus

Morphine (p 3853)
Miosis toxic amblyopia and concentric peripheral contraction of visual fields are frequent sequels

Nitrobenzol (p 757)
See *Aniline*

Nitrous Oxide (p 4003)
Dilatation of retinal arteries

Optochin (p 204)
May cause amblyopia contraction of peripheral visual fields and central scotomas

Paradichlorobenzene (p 1592)
Cataract formation

Paraphenylendiamine (p 1592)
Diplopia lacrimation and chemosis may follow

Picric Acid
Yellow vision with loss of blue and violet

Phosphorus (p 729)
Retinal hemorrhages

Physostigmine (p 3374)
Miosis

Potassium Cyanide (p 748)
Fixed dilated pupils with exophthalmos

Quinine (p 519)
Sudden blindness amblyopia contraction of visual fields attentuation of retinal vessels and pallor of disk may result from idiosyncrasy or overdose

Resorcinol (p 3357)
Conjunctivitis

Santonin (p 1896)
Yellow vision

Silver (p 758)
Argyrosis of cornea in chronic poisoning

Salicylates (p 3340)
See *Quinine*

Sulfonamide (p 88)
May cause optic neuritis and transient myopia

Sulfonal (p 3841)
Ptosis extra ocular pareses and diplopia may result

Thallium (p 760)
Optic neuritis optic atrophy loss of brows and lids bilateral central scotoma and cataract formation may be produced

Tobacco (p 3884)
May cause amblyopia and angiospasms

Trichlorethylene (p 760)
Retrobulbar neuritis

Treatment—The appearance of ophthalmic defects possibly due to drugs and chemicals demands immediate discontinuance of the offending substance Antidotal therapy holds little promise sodium thiosulfate has

Carbon Disulfide (p 747)
May cause *photophobia* nystagmus punctate keratitis impaired accommodation micropsia macropsia and monocular diplopia

Bromide (p 3838)
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Dilatation of retinal arteries

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May result in iritis conjunctivitis scleritis or tenonitis

Hemochromatosis (p 1976)
Slate blue pigment near disk

Hypertensive Toxemia of Pregnancy (p 2638)
May cause attenuation of retinal arteries angiospasms papilledema retinal hemorrhages and exudates or retinal detachment

Hyperthyroidism (p 1197)
May be associated with exophthalmos conjunctival edema exposure keratitis corneal ulceration paresis of extra ocular muscles infrequent blinking lid lag diplopia tearing pulsation of retinal arteries weakness on convergence and widened palpebral fissure

Hypoparathyroidism (p 1232)
Blepharospasm and cataract have been observed

Hypothyroidism (p 1191)
May produce puffy and edematous lids xerosis loss of outer third of eyelid or cataract

Jaundice (p 1951)
Sclera icteric

Laurence Moon Biedl Syndrome (p 1166)
Retinitis pigmentosa

Menstruation (p 2483)
Asthenopia edema and rings under eyes

Nephritis (p 2393)
Chemosis retinopathies and amaurosis

Niacin Deficiency (p 616)
Optic neuritis

Niemann Pick Disease (p 1134)
As Tay Sachs disease but yellow color to optic nerve

Normal Pregnancy (p 2617)
Pigmentations of eyelids

Pituitary Neoplasm (p 1153)
May result in bitemporal hemianopsia papilledema and optic atrophy

Schuller Hand Christian Disease (p 1135)
Usually associated with exophthalmos optic atrophy ulcerative keratitis and extra ocular muscle palsies

Tay Sachs Disease (p 1584)
Cherry red spot with white halo at macula and optic atrophy are characteristic

Thiamine Deficiency (p 616)
Conjunctivitis and oculomotor pareses may occur

been useless in our hands for the relief of *arsenical poisonings* atropine *mydriasis* cannot be alleviated by local instillation of pilocarpine and other miotics Injections of thiamine chloride using intravenous doses of 100 to 200 mg may have some efficacy in relieving the manifestations of *alcoholism* (p 3848) Angiospasmoses such as occur with *ergotism* and *nicotinism* may be relaxed by intravenous papaverine (p 3854) or aminophylline (p 3866)

OPHTHALMIC MANIFESTATIONS OF METABOLIC DISORDERS

Adrenal Cortical Deficiency (p 1271)
Enophthalmos

Allergy (p 1648)
May be associated with angioneurotic edema of eyes conjunctivitis vernal catarrh iritis optic neuritis or paresis of extra-ocular muscles

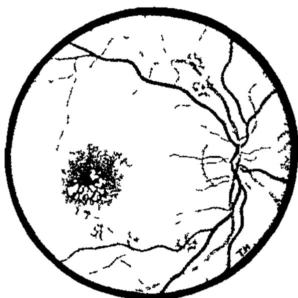


Fig 315 —Diabetic retinopathy *

Ariboflavinosis (p 616)
May cause rosacea keratitis with vascularization of cornea

Cevitamic Acid Deficiency (p 616)
Hemorrhages particularly retrobulbar may follow

Diabetes Mellitus (p 1246)
May produce errors in refraction and accommodation extra ocular palsies iritis cataract retinopathy hemorrhages retinitis proliferans optic and retrobulbar neuritis and lipemia retinalis with haziness and milky appearance of vessels

Gaucher s Disease (p 1133)
Pinguecula in nasal half of conjunctivae

* Gifford, Textbook of Ophthalmology

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May result in iritis conjunctivitis scleritis or tenonitis

Hemochromatosis (p 1976)
Slate blue pigment near disk

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Vitamin A Deficiency (p 616)

May result in xerophthalmia keratomalacia light brown pigmentation of conjunctiva meibomitis blepharitis styes and night blindness

Xanthomatosis (p 1136)

Xanthelasma of lids

Treatment—A certain few of the ophthalmic manifestations of metabolic disorders may respond to specific measures of therapy The *water soluble vitamins* (thiamine chloride riboflavin niacin and cevitamic acid) are given intravenously in large doses for conditions that are possibly attributable to deficiency states *In vitamin A deficiencies* the lacking nutriment is given orally in massive dosage (p 620) *Allergic phenomena* respond symptomatically to injections or local instillations of epinephrine The early use of parathyroid hormone (p 1223) may prevent cataract formation in *parathyroid tetany* (p 1233), the ocular lesions of *hypothyroidism* regress with adequate doses of thyroid extract Emptying of the uterus may be followed by considerable reversal of the changes resulting from *hypertensive toxemia* (p 2638) Correction of the metabolic disorder in *diabetes mellitus* (p 1246) may prevent further damage but has little effect on conditions that have been established The *exophthalmos of hyperthyroidism* (p 1197) may recede after the use of iodides or deracil and following an adequate subtotal thyroidectomy (p 1214) In some instances it may progress despite best intended therapeutic efforts

CHAPTER 80

THE EYE: INFECTIONS INFLAMMATIONS ALLERGY

Ideal management of ocular infection requires identification of the causative organism and localization of the anatomic site of the pathologic process Fully to realize the miracles of anti infective therapy the pathogen must be recognized so that its sensitivity or resistance to the various agencies can be determined Additionally rational therapy is dependent upon knowledge of the nature of the involved tissue Superficial infections of lids or conjunctiva are managed quite differently from similar invasions involving uveal tract or retina where the prognosis is infinitely graver The complete practitioner sets himself the problem of making a *simultaneous etiologic and anatomic diagnosis* Given the identity of the invading organism such as the gonococcus he sets out to discover whether he is dealing with a conjunctivitis susceptible to local treatment or an iritis which must be attacked by systemic methods Contrariwise given an anatomic diagnosis such as conjunctivitis he withholds specific *therapy until he can determine whether he is dealing with an organism* that is sensitive to sulfonamide penicillin or tyrothricin

In keeping with this view of the optimum method of dealing with ocular infection the current chapter has an initial subdivision devoted to the nature of the diverse invading organisms and specific bactericides The second portion of the chapter treats of the inflammatory processes as they are manifested at the various anatomic levels and serves to integrate specific and nonspecific methods of therapy

OCULAR MANIFESTATIONS OF SYSTEMIC INFECTION

OCULAR MANIFESTATIONS OF COCCAL INFECTION

Staphylococcus (p 151)

May cause infection of superficial structures such as lids tear ducts

and sacs and conjunctivae Particularly productive of blepharitis hordeolum and chalazion

Streptococcus (p 157)

May cause erysipelas involving lids cornea optic nerve orbit and meninges Scarlet fever may be complicated by conjunctivitis corneal ulcer and orbital cellulitis Episcleritis iritis and scleritis are encountered in rheumatic fever (p 186)

Pneumococcus (p 199)

May produce contact conjunctivitis or metastatic iritis dendritic keratitis and ophthalmia

Gonococcus (p 217)

Productive of ophthalmia in the newborn Metastatic iritis may be associated with bacteremia or focal infection particularly in the prostate

Meningococcus (p 208)

May produce isolated conjunctivitis or metastatic endophthalmitis ocular paralyses optic neuritis papilledema and amaurosis during bacteremia

Catarrhalis

May be associated with local infections of the lids and conjunctiva

Treatment—The specific treatment of coccal infection of the eye is an embarrassment of riches since the organisms are susceptible to sulfonamide and penicillin whether given locally or systemically Additionally tyrothricin is efficacious in gram positive invasions particularly with the pneumococcus

Superficial staphylococcal infections are best treated with 5 per cent sulfathiazole ointment or 30 per cent sodium sulfacetimide Resistant strains may require the substitution or addition of penicillin by instillation or intramuscular injection and when these agencies fail tyrothricin may be *topically administered*

Streptococcal infections involving the deeper structures or resulting from systemic invasion necessitate oral dosages of sulfonamide if the patient is ambulatory supplemented by parenteral penicillin if there are facilities for injection therapy Excellent results may be anticipated in erysipelas and scarlet fever but the rheumatic manifestations by their very nature are resistant

For *pneumococcic conjunctivitis* of contact origin ophthalmologists place the greatest reliance on topical administration of tyrothricin though local applications of sulfonamide and penicillin may be equally successful Deeper involvements must be managed by oral doses of sulfonamide or parenteral administration of penicillin

Infections with *gonococcus* or *meningococcus* seem best treated by intramuscular injections of penicillin Satisfactory results also may be obtained in all but infections with resistant strains by topical and oral administration of sulfonamide

OCULAR MANIFESTATIONS OF BACILLARY INFECTION

The significance of tuberculous infection of the eye overshadows the remaining bacillary disturbances of the organs of vision None of the ophthalmic structures displays significant immunity to the acid fast invader and experienced ophthalmologists suspect tuberculosis in any chronic inflammatory process particularly if it occurs in a patient who is known to have or have had a Koch bacillus infection elsewhere in the body

B anthracis (p 299)
Malignant pustule may occur around the eyelids

C diphtheriae (p 302)
May cause conjunctivitis optic neuritis post diphtheritic extra ocular palsies and paralysis of accommodation

S dysenteriae (p 243)
Conjunctivitis and iridocyclitis are rare complications

H influenzae (p 396)
May produce conjunctivitis purulent dacryocystitis herpetic keratitis iritis uveitis retinal hemorrhages ocular palsies and optic neuritis

M leprae (p 273)
Leprosy may be associated with anesthetic patches on the lids loss of lashes and eyebrows nodular deformities of the lids conjunctivitis superficial keratitis nodular iritis and optic atrophy

M mallei (p 327)
Glanders may be represented by a primary implant with a pre auricular lymphadenopathy or conjunctivitis

B melitensis (p 314)
Brucellosis may cause iritis iridocyclitis optic neuritis papilledema optic atrophy extra ocular palsies conjunctivitis and hemorrhagic phenomena

H pertussis (p 278)
Cough may be followed by sub conjunctival and orbital hemorrhages

P pestis (p 321)
Plague may be associated with exudative retinitis and retinal detachment

M tuberculosis (p 252)
The tubercle bacillus may produce choroid tubercles ulcero necrotic conjunctivitis sclerosing keratitis interstitial keratitis uveitis retinitis retinal periphlebitis (Eales disease) phlyctenular keratoconjunctivitis (p 1628) uveo parotid fever (Heerfordt s disease) (p 1635) chorioretinitis juxtapapillaris (Jensen s disease) (p 1635) and Boeck s sarcoid with iritis conjunctivitis and uveitis (p 3271)

P tularensis (p 323)

The primary lesion of tularemia may occur in the conjunctiva as an ulcero necrotic nodule with regional lymphadenopathy

E typhosa (p 225)

Typhoid fever may be characterized by corneal ulceration iritis metastatic *choroiditis optic neuritis ocular palsies and retinal* hemorrhages

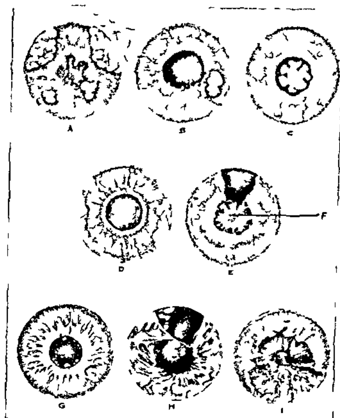


Fig 316—*A* Peracute conglomerate tuberculous iridocyclitis with perforation of the sclera *B* Solitary tuberculoma *C* Subacute nodular or follicular tuberculous iritis *D* Tuberculous iritis of the ciliary region glassy walls of lymphomatous tuberculous nodules *E* Tuberculous iritis involving the pupillary area *F* Occlusion of the pupil *G* Knobs on the pupillary border in quiet cyclitis *H* Quiet tuberculous iridocyclitis with mutton fat precipitates and atrophic changes *I* Anterior synechia after iris bombee and cured tuberculosis

V comma (p 249)

Sunken eyeballs and dullness of the cornea result from the dehydration of cholera

Treatment—Anti infective treatment of bacillary infection of the ocular apparatus is disappointing The sulfonamides and penicillin may be administered locally and parenterally in certain superficial inflammatory processes such as the malignant pustule of anthrax Lesions produced by *P tularensis H influenzae H pertussis M tuberculosis* and the typhoid

Zeeman in Berens The Eye and It Diseases

dysentery group merit therapy with streptomycin (p 106) by topical or parenteral administration Chemotherapy may be given in conjunction with serum therapy in anthrax and diphtheria but the brilliant successes seen in coccal infection cannot be duplicated

OCULAR MANIFESTATIONS OF SPIROCHETAL INFECTION

The lesions of syphilis dominate ocular spirochetal infections Particularly in a known syphilitic the presence of chronic inflammation suggests a local ocular manifestation of systemic invasion Nevertheless the practitioner must remember that the syphilitic is as prone to develop non syphilitic ocular disturbances such as cataract or glaucoma as his Wassermann negative fellows

L icterohemorrhagiae (p 360)
: Infectious jaundice may be associated with conjunctivitis iritis iridocyclitis retinal hemorrhages optic neuritis and icterus of the sclera

Sp minus (p 363)
: The primary inoculum of rat bite fever may occur on the lids Later the patient may develop conjunctivitis and uveitis

B recurrentis (p 357)
: Uveitis iridocyclitis and retinal hemorrhages may be noted in relapsing fever

T pallidum (p 331)
: Syphilis may become manifest through a chancre of the lids orbital periostitis extra ocular paralyses internal ocular paralyses (Argyll Robertson pupil) optic neuritis papilledema primary optic atrophy scleritis interstitial keratitis (in neonatal infection) iritis and choroiditis (p 1632)

T pertenue (p 351)
: Yaws may be accompanied by granular conjunctivitis and secondary contractions resulting in ectropion and exposure keratitis

Treatment—The acute inflammations resulting from spirochetal invasion of the visual apparatus may be expected to yield with miraculous efficacy to the arsenicals (p 116) and penicillin (p 106) The chronic processes do not present a favorable prognosis since many represent irreversible lesions such as optic neuritis Additional therapeutic measures worthy of trial under these circumstances include hyperthermia malarial therapy and injections of tryparsamide

OCULAR MANIFESTATIONS OF RICKETTSIAL AND VIRUS DISEASES

Rickettsial disease is of minor importance in ophthalmic infection but ocular tissues appear to be highly susceptible to virus invasions whether by local implant or systemic dissemination The predominantly local virus infections of the eye are described in detail with the material on conjunctivitis (Beal s disease epidemic keratoconjunctivitis inclusion conjunctivitis and trachoma p 1695) The local manifestations of systemic virus disease are listed below

Anterior Poliomyelitis (p 457)
Bulbar type results in paralyses of extra ocular muscles

Chickenpox (p 420)
Vesicles may appear on the lids conjunctiva and cornea with progression to secondary iritis

The Common Cold (p 391)
Usually associated with suffusion of the conjunctiva and nasolacrimal edema

Epidemic Encephalitis (p 441)
May result in diplopia ptosis paralysis of extra ocular muscles nystagmus Argyll Robertson pupil disturbances of associated movement loss of convergence and paralysis of divergence

Foot and Mouth Disease (p 435)
Often results in conjunctivitis and corneal ulceration

Herpes Febrilis (p 433)
Painless groups of vesicles may appear on lid Healing occurs without *scar formation*

Herpes Zoster (p 435)
Herpes ophthalmicus is a serious infection accompanied by severe pain and vesiculation Lesions of the upper lid accompany involvement of the first division of the trigeminal nerve those of the lower lid indicate involvement of the second division with possible implication of the eyeball Ulceration of vesicles may lead to insensitivity of the cornea iritis, uveitis secondary glaucoma and loss of vision

Lymphopathia Venereum (p 471)
May be associated with follicular conjunctivitis pre-auricular lymphadenopathy uveitis retinal hemorrhages and episcleritis

Measles (p 409)
Early suffusion of lids with conjunctivitis Later keratitis with corneal ulceration may result in permanent impairment of vision Infrequent complications include weaknesses of accommodation optic neuritis and extra ocular palsies

Molluscum Contagiosum (p 422)
Produces umbilicated tumors of lid margins with conjunctivitis

Rubella (p *417*)
In first trimester of pregnancy may produce cataract of the newborn and retrolental fibroplasia

Smallpox (p 424)
The pustules of cornea may result in ulceration residual opacity impairment of vision

Typhus (p 369)
May be accompanied by exudative and hemorrhagic retinitis

Vaccinia (p 428)
Auto contamination of inoculum may produce lesions of lids con

junctiva and cornea Under latter circumstance ulcerative keratitis and impairment of vision may be produced

Treatment—The treatment of the local virus diseases of the eye is discussed with the material on conjunctivitis (p 1616) Encouraging results have been obtained with sulfanilamide in the management of inclusion conjunctivitis and trachoma The ocular manifestations of systemic virus disease present a less rosy prospect but rickettsial infections yield to para aminobenzoic acid

OCULAR MANIFESTATIONS OF MISCELLANEOUS INFECTIONS

The practitioner rarely encounters ophthalmic manifestations of invasions with fungi protozoa and helminths but an important problem is posed by disturbances of the visual apparatus due to focal infection and to spread by continuity particularly from the accessory nasal sinuses The investigation of orbital cellulitis and inflammations of the vascular tunic and neural elements is incomplete unless there has been a meticulous survey of teeth upper respiratory passages and genital tract for the possible presence of a more fundamental lesion

Actinomycosis (p 489)
May cause orbital involvement secondary to lumpy jaw

Acute Disseminated Lupus Erythematosus (p 3599)
Produces eruption on lids and hemorrhages and exudates of retina

Aspergillosis (p 498)
Corneal ulceration is occasionally encountered

Blastomycosis (p 493)
May involve skin of eyelids and conjunctiva Rare iritis

Dermatomyositis (p 3373)
May be associated with pareses of external ocular muscles nystagmus exophthalmos iritis retinitis flame shaped retinal hemorrhages

Erythema Nodosum (p 3377)
Nodular swellings may involve subconjunctival regions

Favus (p 3304)
Rare conjunctivitis but frequent involvement of lids

Filariasis (p 3326)
Parasites in intra ocular tissues or conjunctival sac (Blinding Filaria)

Focal Infection (p 42)
Of particular importance in keratitis iritis iridocyclitis choroiditis uveitis optic neuritis retrobulbar neuritis and scleritis

Infection by Continuity (p 2130)
Inflammation of accessory nasal sinuses of greatest significance in orbital cellulitis optic neuritis and uveitis

Leishmaniasis (p 534)
May cause interstitial keratitis corneal abscess and perforation

Leptothricosis (p 1623)
    Granulations on conjunctiva and enlargement of pre auricular gland (Syndrome of Parinaud) with demonstrable leptothrix

Malaria (p 507)
    Dendritic corneal ulcer with retinal hemorrhages Quinine amaurosis

Myiasis
    Larvae in conjunctivae cause inflammation and occasional corneal ulceration Larvae in vitreous may cause blindness

Pediculosis (p 3131)
    Nits involve lashes

Schistosomiasis (p 537)
    Conjunctival tumors may contain ova

Sporotrichosis (p 495)
    Rare conjunctivitis or keratitis

Teniasis (p 1899)
    Eggs may be deposited in any structure of eye causing severe local inflammation

Thrush (p 1697)
    Rare conjunctivitis

Trichinosis (p 539)
    Chemosis subconjunctival hemorrhage and limitation of movements of eyeball

Trichophytosis (p 3293)
    Rare conjunctivitis or keratitis

Trypanosomiasis (p 531)
    Keratitis of interstitial type with vascularization Uveitis also occurs

Treatment —Local treatment may be of value in many of the miscellaneous inflammatory processes involving the superficial ocular structures Included in this group are the fungous disturbances filariasis myiasis pediculosis teniasis and trichophytosis Most dramatic therapeutic successes are often obtained by elimination of foci of infection and the control of neighboring disturbances particularly the spheno ethmoiditis that is associated *with optic neuritis In the investigation of these latter problems* the practitioner should resort to round table consultation with ophthalmologist and rhinologist

PREDOMINANTLY LOCAL INFECTIONS, INFLAMMATIONS AND ALLERGIES OF THE VISUAL APPARATUS

Infections inflammations and allergies may result in specific elective involvement of the several tissues that make up the ocular structures Prognosis and therapy are greatly influenced by the site of the lesion as illustrated in the remaining material of the present chapter

DERMATITIS OF THE LIDS

See *Analogues of the Dermatoses* (p 1564)

ABSCESS OF THE LIDS

Abscess of the lids usually follows injury or infection of the eyebrows particularly after plucking The free borders of the lids and the cilia are not usually involved even when the abscess is extensive

Continuous *hot wet dressings* and local applications of 5 per cent sulfathiazole ointment are of great value in the early course of the abscess When fluctuation develops a *horizontal incision* is made parallel to the lines of the skin The venous return of the upper lid into intracranial channels suggests the wisdom of instituting prophylactic chemotherapy with *sulfonamide* (p 88) and/or penicillin (p 106)

ULCERS OF THE LIDS

Ulceration of the skin of the lids has ominous implications The lesion may be *vaccinal* (p 428) following immunization but on rare occasions it represents the primary infection of *syphilis* (p 331) *tularemia* (p 323) or *rat bite fever* (p 351) Some lesions are *epitheliomatous* (p 3220) and others are late manifestations of *leprosy* (p 273) or *tuberculosis* (p 252)

The differential diagnosis of ulcerations of the lids must be intensively pursued The recognition of rat bite fever is apparent from the history Tularemia is suggested in patients bitten by deer flies or ticks and in those who have handled the hides of infected rabbits and other rodents Dark field examination (p 45) is required for the identification of the *T pallidum* of syphilis and if this test is not definitely positive a biopsy is indicated to reveal the nature of the inflammatory or neoplastic process

BLEPHARITIS MARGINALIS

Blepharitis marginalis or ciliaris is an inflammation of the margin of the lid It is a very common and recurrent condition characterized by local redness thickening granulation scaling and crusting Itching local soreness and asthenopia are important symptoms but most frequently the patient seeks medical care for cosmetic reasons

The disturbance starts as a simple hyperemia of the lid margin and often is seen in persons of fair complexion In extreme examples the edges of the lids are swollen and yellowish crusts glue the lashes together to cover bleeding ulcers Eventually the lashes fall out or become distorted due to destruction of hair follicles Lid margins become greatly thickened and *trichiasis* and *ectropion* occur (p 1569) *Chronic conjunctivitis* (p 1616) and *recurrent styes* (p 1610) are frequent complications

Etiology —In blepharitis the usual causative organism is *Staphylococcus aureus* or toxic *Staphylococcus albus* (p 151) *Predisposing factors* are said to include errors of refraction poor resistance to infection poor hygienic surroundings adverse occupational conditions irritation from cosmetics and defects in diet Most often in our experience the lesion is independent of these circumstances and seems to occur on some presently unknown constitutional basis

Treatment —Local treatment includes the application of 1 or 2 per cent silver nitrate to the lid margins the *manual expression* of lid glands and removal of scales crusts and diseased cilia Ointments of 1 3000 *bichloride of mercury* *p nicillin* or 5 per cent *sulfathiazole* are applied locally If the condition persists or recurs a culture of the lid

margin is taken and if a pathogenic staphylococcus is recovered *injections of staphylococcus toxoid* (p 78) or *an autogenous vaccine* are given The senior author is convinced that there is a close association between blepharitis and seborrhea sicca (dandruff) It is his experience that the lids will not clear unless scalp treatments are undertaken at the same time (p 3137)

PHTHIRIASIS PALPEBRARUM

Phthiriasis palpebrarum the presence of the *crab louse* (pediculosis pubis) on the eyelashes usually occurs in children and responds readily to inunctions of 3 per cent *ammoniate mercury ointment* (p 3137)

HORDEOLUM (STYE)

Hordeolum is an *acute suppurative inflammation* of one of the glands of Zeis on the lid margin As a result the affected lid and contiguous conjunctival membrane are swollen and the pre auricular gland enlarges *Gentle palpation of the lid margin with a cotton applicator reveals an* especially sensitive spot corresponding to the inflamed gland Within a day or two increasing swelling redness and yellowish discoloration are noted in the area

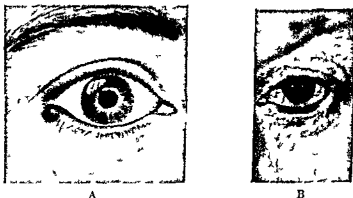


Fig 317—*A* Hordeolum *B* Chronic blepharitis

Etiology—Styes or external hordeola are due to *staphylococcic infection* (p 151) While they occur at all ages they are most common in children or young adults and often appear in crops They are frequently an expression of a lowered state of resistance due to errors in diet or hygiene and they may be associated with an *uncorrected refractive error* In the middle aged recurring styes are seen in uncontrolled *diabetes* (p 1246)

Treatment—*In the incipient stage symptoms may subside after removal of a lash* in the region of the involved gland and applications of penicillin or *5 per cent sulfathiazole ointment* On failure of abortive treatment *hot compresses* are used to bring the stye to a head At this time the conservative wait for the abscess to evacute but the less patient release pus by a horizontal incision using a sharp scalpel It is the experience of the senior author that the policy of watchful waiting' is

followed by fewer recurrences since abscess fluid is more likely to be sterile at the time of spontaneous release

If styes tend to recur injections of *staphylococcus toxoid* (p 78) or *autogenous vaccine* are used if cultures reveal the presence of a toxic staphylococcus The patient is referred to the specialist for the correction of refractive errors but despite best efforts lesions may continue to recur

CHALAZION

Chalazion is a chronic inflammatory enlargement of a meibomian gland A hard swelling of the lid may develop without gross inflammatory symptoms until it reaches the size of a small or large pea The tumor is circumscribed and adherent to the tarsus but not to the skin Eversion of the lid reveals reddening and thickening of overlying conjunctiva which later assumes a grayish yellow appearance In this phase the chalazion is unsightly and productive of conjunctival irritation Eventually there is cyst formation or granulation of the mucosal surface

With secondary infection an internal hordeolum or suppurating chalazion appears The lids become red and swollen the conjunctiva is chem

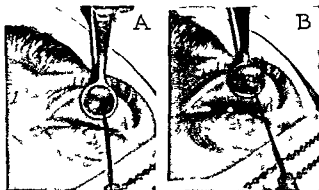


Fig 318—Technic of operation for chalazion A Incision B Curettage

otic pain is so severe that it may be impossible to evert the lid in order to observe the conjunctiva

Treatment—The treatment of the *non infected chalazion* is accomplished by surgical excision (p 1556) If the *secondarily* infected chalazion is seen within the first few days of its onset suppuration may be prevented by expression of discharge through the opening of a meibomian gland Hot compresses are applied and penicillin or 5 per cent sulfathiazole ointment is rubbed into the area In the presence of *associated constitutional symptoms* and with a *hyperacute* or *spreading local lesion* systemic administration of sulfonamide or penicillin (p 106) is advised

When the infected chalazion has localized pus is evacuated through a vertical incision of the conjunctiva or one that is horizontally placed through the skin The lesion promptly subsides with adequate drainage but residual granulation tissue may require attention at a later period Cultures usually reveal a pathogenic staphylococcus

DIFFERENTIAL DIAGNOSIS OF

Disturbances of the Eyelashes and Eyelids

Abnormalities involving the ocular adnexa are usually the concern of the practitioner to whom the patient appeals particularly in communities where there are no special st ophthalmologists

	DIAGNOSTIC FEATURES
Congenital Anomalies	See p 1560
Analogues of the Dermatoses	See p 1564
Physical Mechanical and Chemical Injuries	See p 1569
Cysts and Neoplasms	See p 1566
Inflammations and Infections	Particularly blepharitis hordeolum (tye) and chalazion
Allergies	Contact dermatitis from ocular medications or nail polish
Shaggy Eyebrows	Familial Acromegaly with prognathus and changes in sella turcica
Scant Eyebrows	Hyperpituitarism with giantism or acromegaly Leprosy with anesthetic nodules Albinism with lack of pigment Myxedema with low B M R. and therapeutic response to thyroid extract
Lagophthalmos (Inability to Close Eye)	Facial paralysis Exophtha mos
Ptosis (Drooping of Upper Lid)	See p 1649
Crusting of Lids	Hyper ecretion of glands of Moll Blepharitis marginalis Asthenopsia with refractive error Seborrhea (dandruff) Hordeolum (stye) *Contact dermatitis Measles with characteristic xanthem*
Widening of Palpebral Fissure	With exophthalmos myopia orbital cellulitis and cavernous sinus thrombosis Make local examination Refract and perform exophthalmometry (p 1546)
Narrowing of Palpebral Fissure	Enophthalmos particularly in Horner s syndrome Dehydration ptosis and blepharophimosis
Dark Circles Under Eyes	Familial With fatigue menstruation pregnancy senility hyperthyroidism and adrenal cortical deficiency
Blepharospasm	With burns foreign bodies allergies conjunctivitis *keratitis hypoparathyroidism*, asthenopsia habit spasm chorea and albinism Make local inspection and obtain exudate for smears and cultures Get epithelial scrapings (p 1546)
Ecchymosis (Black Eye)	Following direct trauma fracture of skull pertussis epilepsy and hemorrhagic diatheses If no direct injury get skull x ray and hemogram (p 3704)
Ulcers of Lids	*Blepharitis marginalis epithelioma* primary syphilis tularemia and glanders In doubt examine by darkfield microscopy and by direct smears and cultures (p

D

Edema of Eyelids	Insect bites and burns Inflammations and infections of lids conjunctiva sclera cornea lacrimal passages and lacrimal glands Contact dermatitis particularly with cosmetics Glaucoma with increased intracranial tension Orbital cellulitis and panophthalmitis Cavernous sinus thrombosis with bacteremia Nasal accessory sinusitis particularly of sphenoids and ethmoids with x ray changes Pertussis with paroxysmal cough Measles varicella and variola with characteristic rash Trichinosis with eosinophilia Angio neurotic edema of allergic origin Hypothyroidism with low B M R Anemia with characteristic hemogram (p 3704) Nephropathies with characteristic urinary and blood findings (p 2362) Backward failure Nephrosis Water intoxication Salt retention and dermatitis medicamentosa (p 3335)

With recurrence *preventive measures* are instituted The patient is referred to the ophthalmologist for refraction Errors in general hygiene are corrected Injections of staphylococcal toxoid or of autogenous vaccine are begun and 5 per cent sulfathiazole ointment or 1 per cent yellow oxide of mercury ointment is massaged into the lids each night

CHRONIC MEIBOMITIS

Chronic infections of the meibomian glands result in redness and swelling of the lid margin and the appearance of foamy secretion in the conjunctival sac

The lids are expressed frequently to prevent multiple *chalazia* and *blepharitis* The patient is advised to practice nightly inunctions of *5 per cent sulfathiazole* or 0.5 per cent *ammoniated mercury*

TARSITIS

Involvement of the tarsus may result from *syphilitic tuberculous* or *trachomatous infection* The condition becomes manifest as a thickening of the lids with tenseness and redness of the overlying skin With positive serologic tests for syphilis antiluetic therapy (p 340) is instituted Otherwise the patient is referred to the specialist for diagnosis if necessary by examination of smears and biopsy

Local treatment is palliative Hot compresses and antiseptic ophthalmic ointments are used twice daily

DACRYADENITIS

Acute inflammation of the tear glands is extremely rare When present it is manifested by swelling redness and tenderness of the upper temporal margin of the orbit The lesion is treated in the manner of a suppurating chalazion (p 1611) preferably by the consulting ophthalmologist

Mikulicz s Disease —Chronic bilateral enlargement of the lacrimal glands associated with similar processes in the parotid and other salivary glands occurs in Mikulicz s disease (p 1709) The latter is often associated with *leukemia* (p 1100) so that complete blood studies are required

CHRONIC DACRYOCYSTITIS

Chronic inflammation of the lacrimal sac usually follows obstruction of the nasal duct (p 1569) With simple occlusion, the only symptom is tearing With distention and nonpurulent inflammation a *mucocele* develops in the region of the sac and watery or mucoid fluid escapes from the punctum In chronic purulent dacryocystitis pressure upon the distended sac yields pus containing staphylococci streptococci pneumococci or the Friedlander bacillus Persistence of purulent dacryocystitis results in *chronic conjunctivitis* (p 1616) and the threat of serious *corneal inflammation*

Treatment—The patient with dacryocystitis is referred to the consultant *ophthalmologist* *Non operative procedures are attempted by dilatation and irrigation of the lacrimal passages* (p 1557) If the disturbance fails to subside operative interference is advisable *Dacryocystectomy* (p 1557) is the simpler procedure but it may be followed by persistent tearing The more extensive *dacryocystorhinostomy* (p 1557) in which the cavity of the lacrimal sac is joined directly with the nasal fossa, is a more formidable procedure but yields more satisfactory late results

ACUTE DACRYOCYSTITIS

Acute dacryocystitis almost always follows the chronic form of infection (above) On rare occasions it results from extension of infection from the nose or its accessory sinuses The lesion is more properly termed an *acute peridacryocystitis* since it is really a purulent inflammation of the connective tissues that surround the chronically inflamed tear sac

The condition is recognized by swelling redness and edema of the skin that overlies the lacrimal sac There may be associated chemosis pain tenderness and constitutional symptoms Suppuration is manifested by the appearance of a localized area of yellowish discoloration

Treatment—In the early phases of an acute dacryocystitis the lesion is treated with continuous wet dressings The appearance of constitutional symptoms is sufficient indication for systemic chemotherapy using *sulfonamide* (p 88) or *penicillin* (p 106) If the inflammation does not subside the abscess is drained by *incision* which may require induction of *general anesthesia* Delay in evacuation of pus may lead to the formation of a *lacrimal fistula*

ORBITAL PERIOSTITIS

Inflammation of the bone of the orbit and orbital periosteum may be acute or chronic localized or extensive Orbital periostitis usually results from injury tuberculosis syphilis or infection of the nasal accessory sinuses The margin of the orbit is most often involved *Symptoms* consist of localized pain tenderness and swelling A *subperiosteal abscess* may develop with later formation of a *fistula* If the periostitis occurs posteriorly it simulates an *orbital cellulitis* (p 1615) and is treated as such

Treatment—The patient with orbital periostitis requires hospitalization Serologic tests for syphilis are performed radiographs of the skull and nasal accessory sinuses are required and ophthalmologist and rhinologist are summoned in consultation

In the presence of positive evidences for syphilis antiluetic therapy is instituted (p 340) Nonsyphilitic infections are treated systemically with

sulfonamides and penicillin (p 106) Suppuration in the nose or accessory sinuses requires indicated operative procedures

ORBITAL CELLULITIS

Orbital cellulitis may be secondary to *erysipelas* (p 107) or *orbital periostitis* More often however it is observed in children with purulent sinusitis involving *frontals sphenoid* or *ethmoids* (p 2125)

Orbital cellulitis is manifested by inflammatory edema of the lids chemosis protrusion and/or displacement of the eyeball limited ocular motility and diminution of vision if there is involvement of the optic nerve

The course of orbital cellulitis is variable The condition may subside with absorption of exudate or it may progress to suppuration and result in *orbital abscess* The latter requires prompt *evacuation* to prevent seri

DIFFERENTIAL DIAGNOSIS OF

Disturbances of the Orbit

Disturbances of the orbit are always of sufficient significance to warrant specialist consultation

	DIAGNOSTIC FEATURES
Congenital Anomalies	See p 1560
Mechanical Disturbances	Exophthalmos and enophthalmos
Neoplasms	See p 1567
Infections	Orbital cellulitis periostitis osteomyelitis and abscess Get x rays of orbit and nasal accessory sinuses Consult rhinologist and ophthalmologist
Vascular Disturbances	Cavernous sinus thrombosis with bacteremia Occlusion of retinal arteries and veins visible by ophthalmoscopy Arteriovenous aneurysm of internal carotid artery and cavernous sinus with pulsating exophthalmos

ous sequels such as optic neuritis panophthalmitis purulent meningitis or thrombosis of the cavernous sinus (p 2130)

Treatment —The patient with orbital cellulitis requires immediate hospitalization and consultations are required with ophthalmologist and rhinologist *Chemotherapy* with sulfonamides and/or penicillin (p 106) is instituted but not to the exclusion of necessary *surgical procedures* such as drainage of the orbital abscess or operations designed for the relief of the more fundamental *suppurative processes in the nose and its accessory sinuses*

TENONITIS

Inflammation of Tenon s capsule occurs rarely and is of obscure etiology It may be associated with gouty and rheumatic diatheses Tenonitis may follow *operations for squint* (p 1530) due to contamination of the

operative field It is characterized by extreme chemosis and limitation of ocular motion without displacement of the eyeball

The management of a tenonitis is specialist province Injections of foreign protein and anti infective therapy may be tried With *arthropathies* salicylates may be useful

CONJUNCTIVITIS

Inflammations of the conjunctiva are extremely common and may be caused by a variety of organisms The severity ranges from mere annoyance to total blindness

Etiology —Infection of the conjunctiva may be a purely *local invasion* On rare occasions the inflammatory process is of *metastatic origin* in the course of systemic disease and the conjunctival lesion may represent a portal of entry resulting in generalized dissemination of the invading organism

The list of those organisms which may produce local conjunctivitis includes staphylococcus, streptococcus pneumococcus meningococcus gonococcus M tuberculosis M leprae H influenzae H conjunctivitidis (Koch Weeks) H duplex (Morax Axenfeld) C diphtheriae T pertenue (yaws) the viruses responsible for inclusion conjunctivitis trachoma Beal s follicular conjunctivitis and epidemic keratoconjunctivitis leptothrix and streptothrix

Metastatic conjunctivitis is most often encountered in the exanthematous diseases (roseola rubella and scarlet fever) gonorrhea epidemic cerebrospinal meningitis and bacillary dysentery Conjunctival contamination may result from auto inoculation in vaccinia variola and varicella Finally the conjunctival lesion may prove to be a portal of entry when there is a primary infection due to syphilis, tularemia or glanders

Pathology —The pathology of conjunctivitis is studied under the magnification of the slit lamp Catarrhal membranous purulent and follicular inflammations are observed

Catarrhal Conjunctivitis —Catarrhal conjunctivitis is seen in acute subacute and chronic phases Commoner etiologic causes are *pneumococcus Staphylococcus aureus H influenzae H duplex* (Morax Axenfeld) *H conjunctivitidis* (Koch Weeks) and *Streptococcus haemolyticus*

The *acute phases* are marked by hyperemia mucopurulent discharge redness and swelling of the mucous membranes and the appearance of vascularized papillae in the tarsal region Acute catarrhal conjunctivitis has a marked tendency toward recovery although occasionally it passes into a subacute or chronic phase *Subacute varieties* are frequently due to the Morax Axenfeld bacillus and *chronic lesions* are often associated with the presence of *precipitating factors such as local irritation* disturbances in general hygiene avitaminoses malnutrition and alcoholism Chronic conjunctivitis is often associated with a *chronic blepharitis* (p 1609) and results in the formation of fine infiltrations of the cornea

Membranous or Pseudomembranous Conjunctivitis —Membranous or pseudomembranous conjunctivitis is observed as a result of infections by *Streptococcus haemolyticus* or *C diphtheriae* In either instance the inflammatory process is severe and is often followed by necrosis of the cornea and subsequent scar formation The gravity of membranous conjunctivitis warrants *specialist consultation*

Purulent Conjunctivitis—Purulent conjunctivitis is most frequently of *gonorrheal origin* (p 217) The inflammatory process is hyperacute and may terminate in *blindness* due to corneal involvement Recovery is often associated with *residual opacities* and *cicatricial deformities* which seriously interfere with vision (p 1638)

Follicular Conjunctivitis—The follicular types of conjunctivitis most often are *viral* in origin In *inclusion conjunctivitis* (p 16?3) and *trachoma* (p 1625) it is possible to demonstrate *inclusion forms* in the epithelial scrapings (p 1546) Bacterial stains fail to reveal the presence of the ordinary organisms In trachoma and epidemic keratoconjunctivitis the mucous membrane lesion is accompanied by corneal involvement healing is associated with opacification and diminution of vision

Clinical Manifestations—The generic manifestations of conjunctivitis include a scratchy or sandy feeling in the eyes itching smarting and photophobia Occasionally the onset is announced by sharp *pain* that suggests the presence of a foreign body In the more severe infections the lids feel hot and heavy and large amounts of exudate may cause blurring of vision



A



B

Fig 319—*A* Acute catarrhal conjunctivitis *B* Acute gonorrheal conjunctivitis

Most of the acute examples of conjunctivitis are associated with enlargement of the pre auricular lymph nodes

In *acute catarrhal varieties* the discharge is mucopurulent the mucous membrane is red and swollen and smears and cultures reveal the nature of the causative organism Profuse discharge characterizes the *purulent forms* of conjunctivitis By contrast in *follicular types* the discharge is scant but conjunctival hyperemia congestion and tearing are intense

The course complications and management of conjunctivitis are dependent for the most part upon the nature of the invading organism as described in succeeding paragraphs

Differential Diagnosis—The initial diagnostic problem in acute conjunctivitis is the differentiation of the mucous membrane infection from *disturbances of the uveal tract* (p 1618) and the syndrome of an *acute glaucoma* (p 1578)

Once the diagnosis of conjunctivitis has been established it is necessary to determine the nature of the *causative organism* (p 1619) and the

TABLE 110—DIFFERENTIAL DIAGNOSIS OF CONJUNCTIVITIS IRITIS AND GLAUCOMA

	Acute Conjunctivitis	Acute Iritis	Acute Glaucoma
History Onset Pain Systemic complications	Usually gradual Discomfort sandy feeling but no real pain No systemic complications	Usually gradual Moderate pain in eye radiating to forehead and temple No systemic complications	Sudden Very severe pain in eye radiating over entire sensory distribution of nerve V Vomiting and prostration
Vision	Good	Moderate impairment of vision	Marked impairment of vision
Pre auricular gland	Often enlarged palpable *and tender*	*Not palpable*	*Not palpable*
Secretion	Usually mucopurulent although may be watery Lids stick together after sleep Smear often shows organisms	None or watery	None or watery
Injection	Superficial or conjunctival injection	Ciliary or deep injection	Ciliary or deep injection
Conjunctiva	Palpebral conjunctiva reddened thickened and hyperplastic	Usually normal	Chemosis often present
Cornea	Clear	Clear but may show deposits on posterior surface	Steamy and insensitive
Iris	Clear	Lacking in luster	Muddy with green sheen
Anterior chamber	Normal	Normal depth but cloudy due to exudation	Shallow
Pupil	Normal	Small and irregular	Dilates oval and fixed
Tension	Normal	Usually normal or low	Increased
Ocular tenderness	None	Marked	Very marked
Fundus	Normal	Normal	Glaucomatous cupping

cytology of the secretion Identification of the particular culprit establishes prognostic implications and the therapeutic program

Complications —Conjunctivitis may be associated with local and systemic complications The latter are rarely observed since the conjunctiva acts as an effective barrier to prevent dissemination of infection Exceptions consist of instances of primary infections in *syphilis* (p 331) *tularemia* (p 323) and *glanders* (p 327)

The *local complications* of conjunctivitis may be immediate or delayed The immediate hazard is the occurrence of corneal involvement such as particularly occurs in infections with pneumococcus gonococcus and the viruses of keratoconjunctivitis and trachoma

Late aftermaths are the effects of scarring corneal opacities are seen in keratoconjunctivitis trachoma and gonorrheal ophthalmia Conjunctival deformities are most frequent in trachoma and yaws

Treatment —Conjunctivitis may be treated by preventive and active measures the latter include local topical and systemic methods of therapy

Prophylaxis —Active measures to prevent conjunctivitis are routine procedures in the newborn and in the care of physicians and other medical attendants whose eyes have been contaminated by infectious discharge Before the introduction of newer anti infective agents it was common procedure to irrigate the eyes with normal saline and then instill 1 to 2 drops of 0.5 to 1 per cent silver nitrate After a wait of at least a minute the eyes were again irrigated with saline solution Despite best efforts therapy was often followed by a chemical conjunctivitis of annoying severity so that 25 per cent mild silver proteinate and 10 per cent strong proteinate were often substituted

Table 111 —Laboratory Aids in the Diagnosis of Conjunctivitis

Gram positive coccus	Staphylococcus streptococcus or pneumococcus
Gram negative coccus	Gonococcus or meningococcus
Gram positive bacillus	*C diphtheriae*
Gram negative bacillus	*H influenzae H conjunctivitidis* (Koch Weeks) *H duplex* (Morax Axenfeld) *P tularensis P pestis M mallei* or *B melitensis*
Carbolfuchsin stain (acid fast)	*M tuberculosis* or *M leprae*
Mononucleosis	Epidemic keratoconjunctivitis or Beal s conjunctivitis
Eosinophilia	Vernal conjunctivitis
Epithelial inclusion bodies	Trachoma or inclusion conjunctivitis
Darkfield microscopy	*T pallidum* and *T pertenue* (yaws)
Biopsy	Leptothrix or streptothrix

Equally effectual prophylaxis with lesser irritation can now be effected by 5 per cent sulfathiazole ointment warmed to a liquid consistency a microsuspension of sulfonamide crystals or a solution of penicillin containing 250 to 10 000 units to the cc

Precautions and Isolation —The patient with conjunctivitis must be regarded as an infectious menace He is required to take scrupulous care of hands Disposable tissues dressings napkins and handkerchiefs must be burned without delay Patients with *gonorrheal urethritis* are instructed as to personal hygiene The hands require scrubbing after touching the genitals and dressings are placed in an incinerator or are burned by a flame

Men and women with genital foci of infection are cautioned against the use of public swimming pools lest the contagion be transmitted to the eyes of others

In institutional life the child with conjunctivitis should be placed in strict *isolation* with special nursing care In factories or schools an outbreak of pink eye or virus conjunctivitis requires prompt and stringent action Afflicted individuals are barred from entrance into any public meeting place Tools and apparatus that are handled by many people are immersed in a 1 1000 solution of bichloride of mercury Each student or laborer is warned to scrub his hands thoroughly with soap and water after each fresh operation and on dismissal

Nonspecific Active Therapy—The most important nonspecific factor in the active treatment of acute conjunctivitis is *frequent lavage* of the conjunctival sac This is accomplished by the use of an *eye cup* or applications of *cold compresses* of physiological saline solution or 4 per cent boric acid

Specific Therapy—The indications for specific therapy depend upon the nature of the invading organism as detailed in the material which follows immediately Conjunctivitis may be treated locally or systemically Sulfonamides penicillin streptomycin, tyrothricin silver and zinc are available for topical application Concentration of the therapeutic agent may be increased by iontophoresis (p 1550), sulfonamide and penicillin may be introduced into the eye by direct injection under specialist supervision For specific systemic treatment the physician has the choice of sulfonamide and penicillin With the more serious and resistant infections all methods are combined

Staphylococcic Conjunctivitis—Conjunctivitis caused by the staphylococcus is very common and is usually observed as the *acute catarrhal type* of inflammation with a tendency to *chronicity* The causative organism may be demonstrated in smears and by culture The condition responds well to the generic treatment for conjunctivitis augmented by local applications of penicillin or 5 per cent *sulfathiazole ointment* Complications are rarely observed if treatment is continued for several weeks after acute symptoms have subsided

Streptococcic Conjunctivitis—Streptococcal conjunctivitis is seen relatively infrequently It may be manifested by an *acute catarrhal* or a *membranous* inflammatory process The bacteriological diagnosis is clearly apparent from the examination of smears and cultures The condition is managed in the manner of a staphylococcic invasion

Pneumococcic Conjunctivitis—Pneumococcic conjunctivitis is usually of the *acute catarrhal* variety and may be associated with *multiple subconjunctival hemorrhages* and *corneal ulceration* The pneumococcus is easily demonstrable in smears and cultures The condition responds promptly to local applications of *sulfonamide* or *tyrothricin* (30 mg per 100 cc) These agents have replaced the topical use of ethylhydrocupreine hydrochloride (optochin)

Meningococcic Conjunctivitis—Meningococcic conjunctivitis may occur in the course of a meningococcemia or as a purely local extra meningeal infection when meningococcal infections are rampant It appears as a hyperacute mucopurulent conjunctivitis indistinguishable from other more benign types It can be diagnosed by smears or scrapings when the organisms are exceedingly profuse

Meningococcal conjunctivitis responds to local sulfonamide therapy Internal administration of sulfonamides and injections of penicillin prevent generalized complications or the development of a carrier state

Gonorrheal Ophthalmia —Direct implant of the gonococcus into the conjunctival sac produces a *hyperacute type* of purulent conjunctivitis that may terminate in *blindness* After an incubation period of several hours to three days the lids appear swollen red and tender The conjunctiva has a bright velvety appearance pain is considerable and associated with a watery or slightly blood tinged discharge Organisms are demonstrable in epithelial scrapings but not in pus Constitutional symptoms such as fever malaise and chilliness may be present On or about the fourth or fifth days the swellings of lids and conjunctiva diminish discharge becomes frankly purulent and abundant and organisms are clearly demonstrable in smears and culture

In the era that preceded anti infective therapy complications were the rule in a gonorrheal conjunctivitis *Corneal ulcerations* (p 1626) were observed perforation often resulted in *panophthalmitis* and *loss of the eye* and healing was associated with *cicatricial deformities* and *corneal opacities* (p 1629)

Ophthalmia Neonatorum—The most hideous type of gonorrheal conjunctivitis is *ophthalmia neonatorum* which becomes apparent on about the second or third day after birth Both eyes show marked swelling of the lids chemosis purulent discharge and corneal ulceration Organisms are readily demonstrated by examination of smears and cultures Besides the gonococcus ophthalmia neonatorum may be due also to staphylococcal streptococcal and pneumococcal invasions or to an attack of inclusion blennorrhea (p 1623)

Treatment—The wide adoption of the Crede method of prophylaxis and therapy with sulfonamides and penicillin have removed most of the threat of gonorrheal ophthalmia *Prevention* is accomplished in the new born by the immediate instillation of penicillin 5 per cent sulfathiazole ointment a microsuspension of sulfonamide crystals or 1 or 2 drops of 0.5 to 1 per cent silver nitrate *Active treatment* consists of local and systemic administrations of sulfonamide (p 88) or penicillin (p 106) The occasional presence of sulfonamide resistant strains and drug toxicity makes penicillin the preparation of choice

Influenzal Conjunctivitis —Influenzal conjunctivitis is usually of the *acute catarrhal variety* It is relatively benign and rarely accompanied by complications The organism may be demonstrated in smears and cultures *Therapy with streptomycin may prove specific*

Diphtheritic Conjunctivitis —The diphtheria bacillus is capable of producing a *membranous type* of conjunctivitis associated with a severe inflammatory reaction The diagnosis is established by demonstration of the organism in smears and cultures The presence of the condition requires the introduction of *diphtheria antitoxin* (p 310) in the manner of diphtheritic inflammations of the nasopharynx Local treatment is accomplished by palliative measures and application of penicillin ointment

Koch Weeks Conjunctivitis (Pink Eye) —The conjunctivitis that is caused by the Koch Weeks bacillus (*H conjunctivitidis*) occurs in *epidemic form* (Pink eye) There is an incubation period of thirty six hours and the attack usually lasts about two weeks Slim *gram negative rods* are

demonstrable in smears and cultures Excellent responses follow the generic treatment for acute conjunctivitis (p 1619) combined with the local use of 5 per cent *sulfathiazole ointment*

Morax Axenfeld Conjunctivitis (Angular Conjunctivitis)—The Morax Axenfeld type of conjunctivitis is usually of the *subacute catarrhal* variety The organism (*H duplex*) shows a *predilection for involvement of inner* and outer *canthi lid margins* and surrounding *skin* This type of angular conjunctivitis is benign and is associated with a stringy mucopurulent discharge that is never very abundant *An occasional corneal ulcer* complicates the conjunctival infection

The Morax Axenfeld bacillus is demonstrable in smears and cultures (p 1619) The organism apparently secretes a protein dissolving ferment which acts by macerating epithelium The application of solutions of 0 05 to 0 5 per cent *zinc sulfate* acts as a specific The efficacy of the preparation is due to inhibition of proteolytic ferment rather than any bactericidal action

Dysentery Conjunctivitis—Late in the course of bacillary dysentery (p 243) a simple *catarrhal conjunctivitis* may be observed The infection is obviously metastatic since organisms are not demonstrable by spread or culture Local therapy is attempted with sulfonamide since *secondary uveitis* (p 1632) sometimes develops within one or two weeks after the onset of the conjunctivitis

Tularemia Conjunctivitis—The *primary infection* of tularemia may be observed in the conjunctival sac Ordinarily the patient gives a history of tick bite or of handling the hide of a deer or a rabbit The *P tularensis* is demonstrable in smears or cultures (p 323) Specific antibiotic treatment with streptomycin is indicated (p 322)

Glanders Conjunctivitis—The primary lesion of glanders may occur in the lids or conjunctiva There is usually a clear history of handling horses *M mallei* may be grown on proper culture media (p 327) and is demonstrable in smears (p 1619) *Treatment* is symptomatic

B Granulosis Conjunctivitis—The bacillus granulosis of Noguchi may produce a *chronic follicular conjunctivitis* in children and young adults The infection is characterized by its mildness and the tendency of follicles to appear on the lower border of the lid The condition runs a benign course with complete restoration to normal Corneal complications and scarring are not observed *Treatment* is palliative and many ophthalmologists believe that the Noguchi organism is a secondary invader that appears in an *inclusion blennorrhea* (p 1623)

Syphilitic Conjunctivitis—The *primary lesion* of syphilis occasionally occurs in the conjunctival sac The clinical characteristics of the chancre are more often conspicuously absent The diagnosis is established once suspicion is aroused by *darkfield findings* (p 45)

A conjunctival chancre requires intensive systemic chemotherapy (p 340) using *arsenicals* or *penicillin*

Yaws Conjunctivitis—A granular conjunctivitis is often associated with yaws (p 351) With subsidence of the inflammation there may be *scarring* and *deformity* of the lid The diagnosis is made on demonstrating *T pertenue* by *darkfield examination* (p 45) *Treatment* is accomplished with the systemic use of penicillin or arsenicals (p 340)

Exanthematous Conjunctivitis —Exanthematous conjunctivitis is an acute catarrhal inflammation that occurs in *roseola rubeola* and *scarlet fever* In roseola the conjunctivitis precedes the cutaneous eruption and occurs simultaneously with Koplik spots (p 410) Palliative treatment is all that is required for the local lesion

Parinaud s Oculoglandular Syndrome —Parinaud s syndrome is characterized by unilocular granulomatous conjunctivitis and great enlargement of the pre auricular lymph glands Most cases appear to be due to a leptothrix infection although the organisms of tularemia tuberculosis lymphopathia venereum and syphilis and yeasts have been shown to be etiological agents Excision of the granuloma is indicated if the lesion fails to yield to sulfonamide and penicillin therapy

Inclusion Conjunctivitis (Inclusion Blennorrhea Swimming Pool Conjunctivitis) —Inclusion conjunctivitis is an acute conjunctivitis that is known as inclusion blennorrhea in the newborn and as swimming pool conjunctivitis in the adult

Etiology —The condition is caused by a filtrable virus similar to that found in trachoma The virus is of genital origin and the reservoirs of infection are probably situated in male urethra and female cervix Epithelial scrapings stained by the Giemsa technic reveal epithelial cell inclusions and free elementary bodies 0 2 microns in diameter The disease has been reproduced by bacteria free suspensions of elementary bodies

Clinical Manifestations —The incubation period of inclusion conjunctivitis is from 5 to 10 days The inflammatory process is most marked in the lower lids In the adult a severe acute follicular conjunctivitis with pre auricular gland enlargement occurs In infants due to absence of lymph follicles an intense papillary conjunctivitis with chemosis and swelling of the lids is encountered In both types a profuse mucopurulent discharge is present The cornea is never involved

Absence of gonococci in smears and the longer incubation period differentiate inclusion blennorrhea from gonorrheal ophthalmia In the adult the involvement of the lower lid distinguishes it from trachoma

Course and Treatment —Until the advent of sulfonamide therapy inclusion conjunctivitis persisted in attenuated form for periods up to six months With local and systemic sulfonamide therapy inclusion conjunctivitis responds rapidly In many cases of inclusion blennorrhea local therapy with 5 per cent sulfathiazole ointment is sufficient to produce cure in a week as lack of tearing in infants maintains a high concentration of the drug in the conjunctiva

Beal s Conjunctivitis —The acute follicular conjunctivitis of the type described by Beal occurs in mild *epidemic form* It is characterized as an acute inflammation with edematous swelling more marked in the lower lid The bulbar conjunctiva is but slightly affected while the palpebral membrane especially in the lower fornices is studded with large follicles Considerable enlargement of pre auricular glands is always present

The diagnosis of Beal s conjunctivitis is suggested by the non purulent nature of the secretion and the demonstration of *mononuclear cells* in epithelial scrapings Cultures are sterile or contain secondary invaders of little significance The etiological agent is probably a virus

Beal s conjunctivitis reaches its peak in three to six days and then

subsides in one to three weeks The inflammatory process is self limited Corneal complications are not encountered and *symptomatic therapy* suffices Local instillations of 0 25 to 0.5 per cent silver nitrate and 0.25 to 1 per cent zinc sulfate may hasten healing

Vernal Conjunctivitis —See p 1650

Epidemic Keratoconjunctivitis —A virulent type of keratoconjunctivitis has been encountered *in epidemic form The onset of the infection is an*

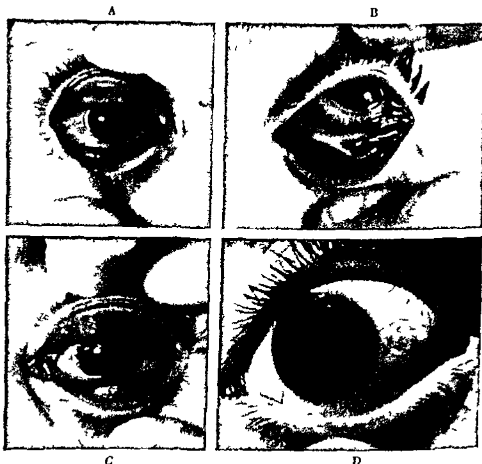


Fig 3 0—Epidemic keratoconjunctivitis *A* Note typical hyperemia and swelling of the palpebral and ocular conjunctiva The acutely inflamed appearance with absence of purulent d scharge is characteristic of this supposedly virus infection *B* A pseudomembrane on the palpebral conjunctiva *C* Note the hyperemia glassy edema and *follicul tis of the palpebral* conjunctiva *D* Corneal opacities complicating epidemic keratoconjunctivitis Note the milky nebulae in the cornea *

nounced by varying symptoms and signs often identical with those of less intense varieties of acute conjunctivitis Hyperemia and swelling of the *palpebral conjunctiva* are noted The patient complains of irritation and a sandy feeling suggesting the presence of a foreign body Tearing may be intense After twelve to thirty six hours the *bulbar conjunctiva* becomes congested and hyperemic the lids appear edematous and a watery

* *Courtesy of Dr* Joseph G Molnar and of Therapeutic Notes Parke D Co

secretion becomes manifest At this time scrapings reveal *mononuclear cells* leukocytes and bacterial organisms are conspicuously absent and cultures are sterile

After about a week the amount of lid edema may be so extreme that it is impossible to open the eyes A pseudomembranous inflammation is observed and if the cornea can be examined *subepithelial opacities* may be noted A dull *fronto occipital headache* is a relatively constant complaint *Pre auricular lymphadenopathy* is accompanied by swelling of *submaxillary and cervical nodes* The condition is differentiated from Beal s conjunctivitis (p 1623) by the presence of the corneal complications

The course of epidemic keratoconjunctivitis is protracted *Corneal* opacities remain long after the acute condition has subsided and may be permanent

Treatment—The present treatment of epidemic keratoconjunctivitis is purely symptomatic Specialist consultation is mandatory Injections of *convalescent serum* have been utilized with reported success *Sulfonamide*



Fig 8 1—Trachoma Early hypertrophic stage

and *penicillin therapy* is worthy of trial in view of the protracted course of the disease and its unfortunate aftermaths

Trachoma—Trachoma causes an appalling amount of suffering blindness and economic loss throughout the world The infection is overwhelmingly associated with poverty and lack of cleanliness It is almost universal among the natives along the eastern Mediterranean especially in Egypt Palestine Iraq and Persia It is very frequent in North Africa Russia Poland Hungary Japan China Mexico Northern Brazil and Argentina In the United States it is fairly common among native Americans living in a zone that reaches from the Alleghenies to Kansas and Oklahoma including eastern Kentucky Tennessee Virginia West Virginia southern Illinois southern Indiana and the Carolinas Ten per cent of the Indian population of the United States have trachoma but Negroes seem to have a definite immunity

Etiology—Trachoma is caused by a *filtrable virus* which can be seen microscopically in an early case as an epithelial cell *inclusion body* similar to that found in *inclusion conjunctivitis* (p 1623) The organisms are found in epithelial scrapings and occur intra and extra cellularly

subsides in one to three weeks The inflammatory process is self limited Corneal complications are not encountered and *symptomatic therapy* suffices Local instillations of 0 25 to 0.5 per cent silver nitrate and 0 25 to 1 per cent zinc sulfate may hasten healing

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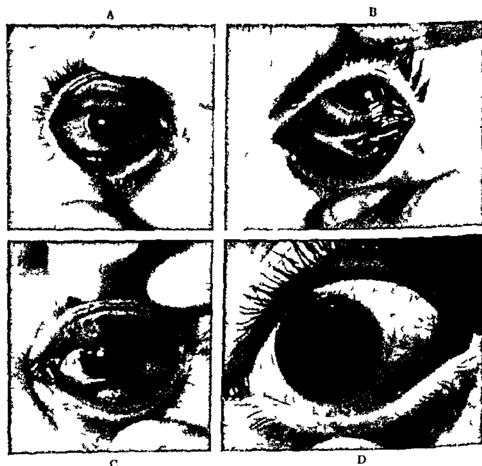


Fig 390 —Epidemic keratoconjunctivitis *A* Note typical hyperemia and swelling of the palpebral and ocular conjunctiva The acutely inflamed appearance with absence of purulent discharge is characteristic of this supposedly virus infection *B* A pseudomembrane on the palpebral conjunctiva *C* Note the hyperemia glassy edema and folliculitis of the palpebral conjunctiva *D* Corneal opacities complicating epidemic keratoconjunctivitis Note the milk nebulae in the cornea *

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* Courtesy of Dr Joseph G Molner and of Therapeutic Notes Parke Davis & Co

temic toxic and infectious processes The lesions are usually chronic and resistant to treatment

Actinic keratitis a variant of punctate inflammation results from exposure to ultraviolet light and the glare of snow klieg lights or an arc flash

Herpetic Keratitis—Vesicles of the cornea are seen in herpes simplex herpes zoster smallpox chickenpox and vaccinia They have been observed also in malaria typhoid fever following protein shock therapy and after treatment with diathermy

The usual corneal appearance is that of an acute superficial *vesicular keratitis* When the lesion assumes an arborescent appearance it is described as a *dendritic keratitis* Vesicular lesions of the cornea respond well to local applications of Tincture of Iodine and Glycerin

Corneal Ulcers—Ulceration of the cornea may result from local or systemic disturbances The diagnosis of the condition is aided by the green staining of the denuded area when *fluorescein* is locally applied

The normal corneal epithelium is an efficient barrier to the penetration of most micro organisms with the exception of the gonococcus and diphtheria bacillus When infiltrations and necrosis occur the ulcer may progress over the cornea (*serpent ulcer*) or it may penetrate deeper into the corneal stroma Damage to Bowman s membrane or stroma results in permanent *opacification*

Hypopyon Keratitis—When an extensive and penetrating corneal ulcer is sufficiently toxic the associated iridocyclitis results in an exudation from iris and ciliary body Pus collects in the anterior chamber (*hypopyon*) where it remains sterile unless corneal perforation occurs

Neuroparalytic Keratitis—After injury to the ophthalmic branch of the trigeminus the cornea becomes infiltrated and may ulcerate Trophic disturbances are prone to progress to perforation and loss of the eye unless the lid can be kept closed

Diffuse Parenchymatous or Interstitial Keratitis—Interstitial keratitis is an inflammation of the stroma of the cornea It is most often a manifestation of neonatal syphilis but it may also be encountered in tuberculosis focal infection leprosy trypanosomiasis and leishmaniasis In benign instances there may be almost complete clearing of the opacity though obliterated blood vessels remain permanently In more severe cases associated uveal tract inflammation and incomplete absorption of corneal opacities result in permanent and often serious impairment of vision

Keratitis Profunda—Keratitis profunda is an inflammation of the deeper layers of the cornea It occurs in adults and is associated with only moderately irritative symptoms Usually the disturbance clears within a few weeks The cause is usually unknown but it may follow trauma and has also been seen with upper respiratory infections and malaria

Keratitis Disciformis—In keratitis disciformis a disk shaped opacity is seen in the middle layers of the cornea The condition is of unknown etiology

Sclerosing Keratitis—In the course of a *scleritis* (p 1631) the cornea may become involved by a vascularized triangular shaped opacity with apex toward the center of the orbit This lesion may become very exten

Metabolic Disturbances and Poisoning
May be encountered with xerosis keratomalacia and avitaminoses In conjunction with Schuller Hand Christian disease and hyper thyroidism From exposure to carbon disulfide and chrysarobin

As Local Manifestation of Systemic Infection
May complicate tuberculosis leprosy syphilis yaws herpes simplex herpes zoster measles smallpox chickenpox vaccinia malaria trypanosomiasis and leishmaniasis May be due to focal infection

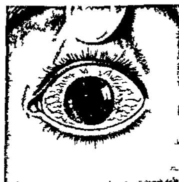
In Allergies
Particularly phlyctenular conjunctivitis

With Increased Intra ocular Tension
In glaucoma

Clinical Manifestations —Inflammation of the cornea is suspected when the patient complains of local pain photophobia lacrimation blepharo spasm and impairment of vision Examination reveals dulness of the cor



A



B

Fig 800 —*A* Interstitial keratitis *B* Herpetic keratitis (dendritic ulcer)

nea and there appear scattered *dull grey infiltrations* or *spots* which stain green with fluorescein if the epithelium has been denuded Circumcorneal injection in the absence of discharge attests to an infection of deeper layers of the visual organs With keratitis there is always evidence of mild or severe *irritation of the iris* the *pupil* is miotic the iris may be clouded and exudate may be observed in the *anterior chamber* Upon even slight suspicion of corneal or uveal tract involvement the assistance of the ophthalmologist is sought

Superficial Keratitis —Superficial keratitis often accompanies various types of *conjunctivitis* (p 1616) and is also seen with *analogues of the dermatoses* (p 1564) A prominent feature of corneal involvements in *trachoma* is the appearance of the *pannus* (p 1625)

Superficial Punctate Keratitis —Superficial punctate keratitis is char acterized by *dot like superficial infiltrations* which stain with fluorescein Most commonly this condition is associated with chronic conjunctivitis but it may also be seen in avitaminosis allergy focal infection and sys

injections of nonspecific protein (p 1552) penicillin (p 106) or streptomycin (p 103) with the inauguration of hyperthermia (p 1552)

Transplantation of the cornea (p 1557) has been successfully practiced by expert surgeons Patients with opacities of the membrane are advised to consider this type of surgical procedure (keratoplasty)

EPISCLERITIS

The origins of episcleritis are similar to those of *keratitis* (p 1626) The condition is of less moment since it does not hold so serious a threat to vision

The onset of an episcleritis is announced by slight pain in the eye photophobia and lacrimation Examination reveals a dark red or purplish area in the ciliary region The lesion may be slightly raised and tender on pressure It is differentiated from *conjunctivitis* by the fact that instillation of epinephrine fails to cause any blanching The *investigation* of an episcleritis follows along the lines suggested in *keratitis* (p 1626) The



Fig 3 3—Scle it



Fig 3 4—Acute ir t s

commoner causes are *focal infection gout atrophic arthritis allergy tuberculosis* and *syphilis*

Treatment—*Local treatment* consists of the application of hot compresses and instillations of an atropine derivative to maintain dilatation of the pupil If there is considerable pain anesthetic drops and epinephrine (p 1548) give considerable alleviation of distress Empirically salicylates (p 383?) are administered orally in large doses Other *systemic measures* include elimination of foci of infection the use of an autogenous vaccine and desensitization with tuberculin

SCLERITIS

In scleritis there is an involvement of the entire thickness of the sclera The manifestations are those of an *episcleritis* (p 1631) except that the intensity is augmented more extensive areas are involved and the entire limbus may be surrounded by an annular process

Scleritis is usually associated with a *sclerosing keratitis* (p 1629) *secondary glaucomatous change* (p 1581) and involvement of the *u eal tract* (p 1632) After healing of the scleritis the weakened membrane may bulge producing an *ectasia*

Gifford Textbook of Ophthalmol gy

sive and interfere with vision after healing A tuberculous etiology is suspected

Keratitis e Lagophthalmo—Corneal inflammation may result from drying *of the cornea due to incomplete closure of the lids following* exophthalmos or facial nerve paralysis In milder forms it is prevented by the use of protective ointments on retiring Following malignant exophthalmos radical surgery is *required to save the eyes*

Diagnosis—The diagnosis of keratitis and its origin pose joint problems for ophthalmologist and practitioner The *ophthalmologist* is concerned with examination of the visual apparatus and the detection of local phenomena that stand in possible etiologic relationship to the corneal lesion The *practitioner* turns his attention to systemic manifestations whose significance requires interpretation

The recital of eating habits may suggest the possibility of an *avitaminosis* (p 616) Family and personal histories are significant in an *allergy* (p 547) Estimation of the *basal metabolic rate* assists in establishing the diagnosis of *hyperthyroidism* (p 1197) *Sensory examination* of the head and neck reveals other than corneal disturbances in *trigeminal lesions* (p 1481) *Tuberculin reactions* (p 262) and a *chest radiograph* are required with *suspicion of involvement with the acid fast bacillus* (p 252) and *serologic tests for syphilis* (p 337) are performed on blood and spinal fluid before definite commitment as to etiology

In the presence of a keratitis that is otherwise inexplicable the possible significance of *focal infection* (p 42) is investigated *Dental roentgenograms* are taken *vitality tests* are made and an opinion is required from the *dental surgeon* (p 1681) relative to possible foci that are not uncovered in such a survey Roentgenograms also are made of *the nasal accessory sinuses* but the fact that these reveal nothing of a positive nature should not deter the practitioner from referring his patient to the rhinologist *for local inspection and diagnostic lavage of the antrum* (p 2128)

Treatment—The *local treatment* of the keratitis is specialist province In all but mildest examples the pupil is kept dilated by atropine or a substitute (p 1548) Dark glasses are used to relieve photophobia and protect the membranes Hot compresses are beneficial and soothing in the vast majority of instances and the associated conjunctivitis is treated according to previously *described methods (p 1619) Adhesions between* cornea and conjunctiva are prevented by separating the lids with vaseline introduced at the end of a stirring rod

Systemic therapy in keratitis depends upon the fundamental underlying condition Syphilis requires antiluetic therapy which is instituted with great vigor Many ophthalmologists favor desensitization with tuberculin (p 1551) in keratitis of otherwise unknown etiology High vitamin diets and accessory vitamin feedings can do no harm if there is any *suspicion* of a deficiency Foci of infection are eradicated in the instance of culpable teeth and tonsils disease of the accessory nasal sinus may be *overcome by lavage* or appropriate surgery (p 2128) Smears and cultures are taken from focal areas of infection and pathogens are grown for skin testing and the manufacture of an autogenous vaccine (p 80)

Persistence of keratitis requires more heroic therapy in the nature of

nasal or postnasal discharge (p 2100) and radiopacities The rhinological survey is not complete without *diagnostic lavage of the antrum* and spreads and cultures of material for the detection of a possible pathogen With the completion of these examinations attention is directed to *male* and *female genitals* The *male urethra* (p 2340) is milked and the *prostate* is massaged the *female cervix* is inspected and the *adnexa* are examined bimanually (p 3468)

Uveitis also may accompany or follow obvious infections such as measles scarlet fever variola varicella typhoid fever cholera dysentery malaria rheumatic fever brucellosis influenza pertussis meningococcus meningitis meningococcemia mumps and leprosy

Clinical Manifestations —The clinical manifestations of uveitis vary according to the site of maximum involvement and the relative intensity of the process *Iritis* and *cyclitis* are discussed together as *iridocyclitis* but *choroiditis* is separately considered

Iridocyclitis —With iridocyclitis the patient complains of *pain diminution of vision photophobia* and *lacrimation* The pain in the eye may be most severe and may radiate to forehead temple or cheek Pain of this variety does not occur in *conjunctivitis* an important differential point in diagnosis (p 1618)

Local examination reveals *hyperemia* of the entire eyeball Injection is most marked around the cornea indicating that it is *ciliary* in type The pre auricular gland is not palpable the secretion appears watery and is not purulent The *anterior chamber* is clouded and fine particles or floaters are seen on slit lamp examination An abnormal ray or aqueous flare in the anterior chamber is observed by focal illumination Later *keratitic precipitates* (K P S) are seen The *pupil* is small its reaction is sluggish and it may be irregular if *synechias* have formed When cyclitis is severe there is marked swelling of the upper lid and chemosis and tenderness in the ciliary region intra ocular tension is decreased deposits on the anterior lens capsule are seen in the pupillary zone and the vitreous is hazy

COURSE —An *acute iritis* usually lasts three to six weeks and terminates favorably unless complications such as *secondary glaucoma* (p 1581) are encountered The *chronic types of iritis* are seemingly benign but they may be persistent and recurrent until finally the patient is left with a badly scarred eye complicated by *cataract* (p 1592) or a *glaucoma* (p 1578)

Acute iridocyclitis follows the same course as acute iritis but it is more severe and late results are more disturbing In addition to cataract formation *detachment of the retina* (p 1573) and *atrophy of the eyeball* may result

Chronic cyclitis or uveitis occurs most often in young adults Its onset is insidious and the condition may not be called to the attention of the physician until serious damage has occurred The usual presenting complaint is a *vitreous haze* or a diffuse dust like *speckling of the vitreous* which causes interference with vision

Choroiditis —The subjective symptoms of choroiditis are limited to *visual disturbances Pain* is conspicuously absent and the defect in vision escapes the patient s notice for a long period of time The herald manifestations are observations of flashes of light (*photopsia*) *vitreous opacities*

The presence of scleritis requires *specialist consultation* The investigation of the condition and treatment follow along the lines established for a *keratitis* (p 1626) Many ophthalmologists lay great stress upon the importance of tuberculosis as an etiologic factor Both scleritis and episcleritis occur in association with *atrophic arthritis* (p 2910) and other arthropathies

UVEITIS

The uveal tract is made up of iris ciliary body and choroid Inflammatory disturbances of components of the uveal tract are very similar and rarely occur in isolated form *Iritis* is usually associated with *cyclitis* cyclitis rarely exists without iritis and each produces or results from *anterior choroiditis*

Etiology—A wide variety of etiologic factors may result in the production of a uveitis Local causes include *analogues of the dermatoses* (p 1564) local trauma resulting in *sympathetic ophthalmia* (p 1569) and spread of *infections* from *conjunctiva* or *cornea* (p 1626)

Metabolic Causes—Much more often uveitis results from systemic metabolic or infectious mechanisms Considerable difference of opinion exists as to the relative importance of each factor Older writers were impressed with the *metabolic origins* of uveitis The ocular lesion was said to occur most often in the *gouty* the *rheumatic* with *intestinal autointoxication* in *nephritis* and in *diabetes mellitus* It is our opinion and experience that these factors are of minor significance

Infections—There is increasing belief that uveitis is the result of *systemic infection* but again a difference of opinion exists as to the relative importance and the frequency with which individual factors are participants Older clinicians were impressed with the significance of syphilis but this is negligible in present day practice Present opinion is divided as to the relationship between tuberculosis and focal infection One large group of ophthalmologists believes that *tuberculous uveitis* is exceedingly common It is their opinion that the uveal tract may be involved without significant tuberculosis elsewhere Their basis for the diagnosis of tuberculosis rests upon the results of the tuberculin reaction *therapy is* directed at desensitization with that substance (p 1551)

Our experiences favor the paramount importance of *focal infection* We are not greatly impressed by the tuberculosis theory *nor do we have* great faith in the protracted administration of tuberculin for purposes of desensitization It is our contention that an adequate search for foci of infection *is rarely unsuccessful in the discovery of a possible nest* Therapy is conducted in optimum manner by attention to the relationship between distant and local lesion

At risk of repetition the technic of seeking a focus of infection is again summarized Roentgenograms are taken of *teeth* and *nasal accessory sinuses* The *dental surgeon* is consulted for visual examination of the *gums vitality tests* and *peri apical explorations* of suspicious teeth for diagnostic purposes and to obtain material for bacteriologic smears and cultures The examination of the *tonsils* is scrupulous remembering that the most innocent appearing organ may have an abscess in its center The *rhinologist s* opinion of the nose and throat is essential particularly in the presence of gross abnormalities such as *nasal obstruction* (p 2732)

nasal or postnasal discharge (p 2100) and radiopacities The rhinological survey is not complete without *diagnostic lavage of the antrum* and spreads and cultures of material for the detection of a possible pathogen With the completion of these examinations attention is directed to *male* and *female genitals* The *male urethra* (p 2340) is milked and the *prostate* is massaged the *female cervix* is inspected and the *adnexa* are examined bimanually (p 3468)

Uveitis also may accompany or follow obvious infections such as measles scarlet fever variola varicella typhoid fever cholera dysentery malaria rheumatic fever brucellosis influenza pertussis meningococcus meningitis meningococcemia mumps and leprosy

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metamorphopsia (distortion of images) *macropsia* (enlargement of images) *micropsia* (diminution of images) and *scotomas*

In acute choroiditis the ophthalmoscope reveals pale yellow or greyish white *fluffy areas* with ill defined edges Retinal vessels appear normal unless there is an associated *retinitis* (p 1637) After a variable time the exudate organizes fibrous tissue is formed and the choroid undergoes atrophy As a result of these changes the *white sclera* shines through and gives the lesion a dead white appearance *Pigment* is frequently deposited in or around the healed areas The presence of *vitreous opacities* suggests that there has been additional major involvement of the ciliary body

Choroiditis rarely occurs as an isolated lesion most often it is associated with *retinitis* Its complications include *uveitis optic neuritis* with secondary atrophy *cataract formation* and *sclerochoroiditis*

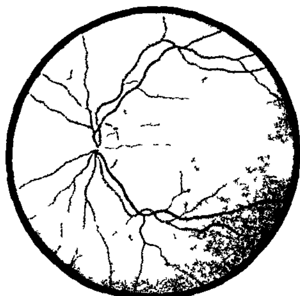


Fig 395 —Acute chorioretinitis *

DIFFUSE CHOROIDITIS —Diffuse choroiditis which is relatively rare consists of the coalescence of patches of exudate with involvement of the greater part of the fundus the retina appears edematous and cloudy eventually there is organization and ophthalmoscopy reveals white scarred areas over which the normally appearing retinal vessels course With *deposition of pigment* secondary pigmentary degeneration occurs which simulates the primary pigmentary degenerations of the retina (p 1592)

DISSEMINATED CHOROIDITIS —The disseminated type of choroiditis is said to be *syphilitic* (p 331) The entire choroid presents numerous round or irregular foci *Vitreous opacities* are present together with a certain amount of edema of the *optic disk* which later may become *atrophic* Massive choroiditis occurs in toxoplasmosis (p 535) particularly in new born infants

* Gifford Textbook of Ophthalmology

CIRCUMSCRIBED EXUDATIVE CHOROIDITIS.—In circumscribed exudative choroiditis one or more large foci are seen to be superficial or deep. The *juxtapapillary choroiditis of Jensen* is an inflammation that is just adjacent to the disk. It is associated with a sector-shaped defect of the visual field, thus differentiating the condition from *optic neuritis* (p. 1641) or *congenital medullation of nerve fibers* (p. 1563).

MACULAR OR CENTRAL CHOROIDITIS.—Macular choroiditis involves the choroid in the region of the macula. Since the retina is thin in this area there is considerable edema and elevation of the membrane and a *central scotoma* appears with marked *loss of vision*.

Subacute and Chronic Uveitis.—Subacute and chronic uveitis include *iritis*, *iridocyclitis* and *choroiditis*. In these inflammations there is limited destruction of tissue, the lesion tends to remain focal, exudation is slight and the cellular reaction is usually of the mononuclear variety. *Exudates* appear as fine cellular *precipitates* on the posterior surface of the cornea. Dust-like *opacities* appear in the vitreous and abundant outpourings of large amounts of *fibrin* cause adhesions to bind the iris to the lens or form a cyclitic membrane behind the lens.

The choroidal changes consist of exudation with mononuclear cellular reactions. The end results of uveal inflammation are *atrophy of the eyeball*, *secondary glaucoma*, *cataract formation*, *detachment of the retina*, *optic atrophy* and *anterior or posterior synechiae* in which there are adhesions respectively to the cornea or lens.

Suppurative Uveitis.—Suppurative uveitis is usually of exogenous origin though it may occur endogenously in the course of an abscess or a generalized infection. Localization of the suppurative process to the choroid or the posterior portion of the uvea gives rise to *endophthalmitis* terminating in the formation of an *abscess of the vitreous*. The latter is suspected by the *yellowish reflex* to the interior of the eye. Endophthalmitis may result in atrophy of the eyeball characterized by softening, detachment of the retina and the formation of massive scar tissue in the vitreous. With involvement of the *anterior uvea* the suppurative uveitis becomes more violent. With involvement of all of the structures of the eyeball a *panophthalmitis* develops.

The cardinal characteristics of suppurative uveitis include intense *pain* in the eyeball, *protrusion*, the formation of *pus* within the eyeball, *perforation* and *phthisis bulbi* in which the eye shrinks after the perforation.

Uveoparotid Fever (Heerfordt's).—Uveoparotid fever is an infection which is marked by chronic inflammation of parotid gland and uvea. It is usually accompanied by chronic iridocyclitis, unilateral facial paralysis, lassitude and a subfebrile temperature reaction. Its origin is unknown and treatment is symptomatic.

Sarcoidosis.—The syndrome of Boeck's sarcoidosis (p. 3271) may be accompanied by conjunctivitis, iritis and uveitis. Roentgen therapy may be effective in expert hands.

Diagnosis.—The diagnosis of uveitis is of importance to the practitioner since the lesion requires immediate reference to the *consulting ophthalmologist*. The distinctions between *acute conjunctivitis* and *acute glaucoma* are summarized in the chart on page 1618.

Treatment.—The treatment of uveitis requires complete cooperation be-

tween ophthalmologist and practitioner Local therapy is the main concern of the former whereas the latter seeks the etiologic mechanism and attempts to deal with more fundamental disturbance

Local Treatment—As soon as the attending physician can be certain of the diagnosis of iridocyclitis even in the presence of an increase in intra ocular tension mydriatics are instilled locally to accomplish dilatation of the pupil rest for the eye and prevention of the formation of adhesions A 1 per cent solution of *atropine sulfate* is administered in drop doses three to six times daily depending upon the pupillary reaction If the patient or the eye appears sensitive to atropine 0 2 to 0.5 per cent *hyoscine hydrobromide* is substituted

Hot compresses are appled locally using saline solution or boric acid These simple applications probably accomplish as much as exposures to *infra-red ray or medical diathermy It is the custom of ophthalmologists* to use liberal doses of the *salicylates* If these have no specific action at least they act as an *analgesic Dark glasses* are prescribed and the patient is best placed in a darkened quiet room

Nonspecific Treatment—While the primary cause of the uveitis is being sought the process of healing may be stimulated by injections of *foreign protein* (p 1552) In the home it is safer to use intramuscular injections of 8 to 12 cc *boiled milk* In institutional practice intravenous *typhoid vaccine* may be employed (p 1552)

In the more severe types of uveitis with progression a trial with *anti infective agents* is worthy of consideration Oral doses of sulfadiazine are administered for a minimum period of three or four days with the usual precautions relative to the discovery of untoward manifestations particularly in the circulating blood (p 88) Concurrently or later intramuscular injections of penicillin may be given (p 106)

Specific Treatment—The most important principles are discovery of a possible focus of infection and prompt institution of remedial therapy It is our opinion that there is less danger of stirring up difficulty by an attack on the focus during the acute phases of the ophthalmological disorder *than in procrastinating with the hazard of permanent damage* to the visual apparatus Infected or even suspicious *teeth* are removed (p 1681) important or essential teeth may be managed by peri apical exploration and amputation *tonsils* are enucleated the *antrums* are irrigated and the sinuses are drained by intranasal or *extranasal surgery* (p 2128) *Smears* and *cultures* are taken from the focus a bacteria free filtrate is obtained for *skin testing immunization* is accomplished by means of an autogenous vaccine (p 80)

Those who favor the theory of the tuberculous origin of *uveitis are* less concerned with seeking and eliminating foci of infection and depend for therapy upon *desensitization with tuberculins* (p 1551) Probatory courses of antibiotic therapy using sulfonamides (p 88) penicillin (p 106) and streptomycin (p 103) merit trial when vision is seriously impaired

Patients with active syphilis receive *antiluetic therapy* (p 340) Generalized *ultraviolet radiation* (p 1550) has been suggested for the management of tuberculous uveitis With persistence of difficulty *roentgen therapy* may be tried

Surgery—The complication of a *secondary glaucoma* (p 1581) may

require the specialist to perform *paracentesis* of the eye A keratome is introduced into the anterior chamber to permit escape of aqueous fluid and the opening is maintained for a period of a week In persistent and recurrent iritis an *iridectomy* (p 1558) may be required At other times the *Lagrange operation* (p 1558) is performed and sclera is removed with iris

RETINITIS

Inflammation of the retina is usually secondary to *uveal infection* (p 1632) Ophthalmoscopy reveals clouding of retina The disk margin is congested and indistinct and exudates and hemorrhages are noted Later proliferative changes with deposition of masses of fibrous tissue result in distortion of the retina due to the formation of grey tumor like masses In final degenerative atrophy of the retina nerve elements disappear blood vessels appear changed and pigment is deposited

The patient with retinitis is referred to the consulting ophthalmologist Meantime efforts are made to reveal the more fundamental causative condition True inflammatory processes are seen in *syphilis* and *tuberculosis* Retinopathies are often associated with *arteriosclerosis* (p 976) *hypertension* (p 900) *toxemias of pregnancy* (p 2638) *diabetes mellitus* (p 1246) and *nephropathies* (p 2362) Petechiae are seen in bacteremias especially subacute bacterial endocarditis (p 1021)

Retinal Hemorrhages —Retinal hemorrhages may involve retina subhyaloid areas or vitreous An end result of organization of the clot is seen in retinitis proliferans

Capillary Bleedings —Hemorrhages into the retina occur essentially from the capillaries The appearance of a hemorrhage in the retina depends on its situation When it occurs in the nerve fiber layer it is striate or flame shaped when situated deeper in the retina it is usually rounded or irregularly shaped The color is usually uniformly red but sometimes there are pale central areas While some retinal hemorrhages are rapidly absorbed and leave no trace of their presence others remain longer and are associated with scarring and white or yellow deposits Hemorrhages are usually asymptomatic but large bleedings situated near the macula may result in interference with vision

The *causes* of retinal hemorrhages include trauma disturbances of the local circulation such as obstruction in venous thrombosis papilledema and subarachnoid hemorrhage the vascular retinopathies of hypertension nephritis diabetes and arteriosclerosis local inflammatory disease of the retina toxic febrile infectious or cachectic states and diseases of the hematopoietic system such as the anemias leukemias purpuras and hemophilia

Before referring the patient with retinal hemorrhage to the ophthalmologist a careful systemic survey is required A *hemogram* may reveal hematopoietic disorders *renal* and *cardiac functional tests* are made *blood chemical analyses* and tests of *bleeding* (p 3706) and *coagulation* (p 3706) are performed In the presence of any striking abnormality the systemic condition is evaluated in reference to the local lesion Otherwise it is the responsibility of the specialist to discover the local etiologic mechanism

DIFFERENTIAL DIAGNOSIS OF

Reductions in Visual Acuity

Reduction in visual acuity may range from minor defects to total blindness The term amblyopia is employed to connote imperfect sensation of the retina without organic lesions involving the visual apparatus When there are demonstrable disturbances of the components that make up the apparatus for the detection of sight the word amaurosis is employed Blindness embraces both amblyopia and amaurosis

	DIAGNOSTIC FEATURES
Psychogenic	Hysterical amblyopia Absence of organic findings
Disturbances of Ocular Adnexa	Conjunctivitis especially trachoma and ophthalmia neonatorum Dacryocystitis particularly in infancy Blinding filariasis
Disturbances of Fibrous Tunic	Keratitis scleritis and episcleritis with corneal ulcerations dystrophies and opacifications noted by slit lamp examination
Disturbances of Vascular Tunic	Choroiditis iritis iridocyclitis uveitis rupture of choroid and sympathetic ophthalmia Refer to specialist for slit lamp examination and fundus observations
Disturbances of Chambers and Refractive Media of Eye	Cataract Glaucoma with increased intra ocular tension Penetrating wounds and hemorrhages involving vitreous with danger of sympathetic ophthalmia
Disturbances of Neural Elements	Retinitis photoretinitis retinitis pigmentosa retinitis proliferans hemorrhage and detachment of retina optic neuritis papilledema senile degeneration of macula and retinoblastoma Refer to specialist for fundus examination
Disturbances of Blood Vessels of Eye	Obstruction of embolism of retinal arteries or veins Refer to specialist for confirmation and treatment
Disturbances of Orbit	Orbital cellulitis periostitis osteomyelitis and abscess Often secondary to inflammation of nasal accessory passages Refer to ophthalmologist and rhinologist Metastatic carcinoma and melanosarcoma Proptosis with exophthalmos
Errors of Refraction and Accommodation	Ametropia presbyopia and asthenopia Refer for refraction
Strabismus	With oculomotor trochlear and abducens paralyses With non paralytic strabismus and phorias Refer to ophthalmologist for diplopia tests
Hemic	Anemias leukemia and thrombocytopenic purpuras with characteristic hemograms.
Cardio-renal Disturbances	Hypertension, hypertensive toxemia of pregnancy and hypertensive encephalopathy associated with nephropathies Get renal function tests and check blood chemistry (p. 3712)

CONTINUED

Systemic Infection	Syphilis of optic nerve with positive serology Meningococcemia with positive blood culture Malaria with demonstrable parasites in blood smears Leprosy with anesthetic nodules Trypanosomiasis in epidemic areas Smallpox and herpes ophthalmicus with vesicular lesions involving cornea Focal infection with second ary uveitis
Contiguous Infection	Of nasal accessory sinuses especially spheno-ethmoids Get x rays and refer to rhinologist for local examination and diagnostic lavage
Organic Neuropathies	Brain tumors abscesses cerebrovascular accidents and injuries involving optic path ways Supplement neurologic examination with x rays of skull and spinal fluid examina tions Multiple sclerosis with disseminated lesions and pallor of temporal half of disk.
Metabolic Disturbances	Schüller Hand Christian disease in children with diabetes insipidus and osseous lesions Amaurotic family idiocy with cherry red spot at macula Avitaminosis A Uncontrolled acidosis
Poisonings	Alcohol particularly methyl Arsenic Qui nine salicylate optochin aspidium, dinitro phenol (obesity cures) and tobacco Optic atrophy with alcohol and arsenic Cataract formation with dinitrophenol Amblyopia with quinine and salicylate

Preretinal (Subhyaloid) Hemorrhages—Subhyaloid hemorrhages have very characteristic appearances They usually occur near the posterior pole and are single and very large A dark red grapelike mass is seen which is circular and projects anteriorly into the vitreous This type of hemorrhage occurs particularly in *leukemia* (p 1100) and may be a herald manifestation of the condition Its appearance demands careful blood studies (p 3692)

Vitreous Hemorrhages—Any profuse retinal or preretinal hemorrhage may invade the vitreous body When this occurs the patient notes *impairment of vision* which may be complete A large hemorrhage abolishes the red reflex of the fundus and precludes ophthalmoscopic examinations of the interior of the eye Thus any sudden loss of vision in which fundus ex amination is impossible and in which nothing of the interior of the eye can be made out must be considered as due to a vitreous hemorrhage

The introduction of vitreous or spinal fluid may help absorption of vitreous hemorrhage

Retinitis Proliferans—When the blood clot following a vitreous hemor rhage becomes organized a retinitis proliferans develops The ophthalmo scopic picture consists of whitish connective tissue strands containing blood vessels which are derived from the retina and run deep into the vitreous There is serious *diminution of vision* and often ultimate *detach ment of the retina* The condition is most often seen in uncontrolled *diabetes mellitus* (p 1246)

PERINEURITIS

Perineuritis (peripheral interstitial optic neuritis) is essentially a meningitis secondary to basal meningitis or suppurative pansinusitis It produces concentric contraction of the visual fields Treatment is directed at the primary lesion Syphilitic adhesive arachnoiditis requires specific therapy and operative interference by the ophthalmologist

OPTIC NEURITIS

Optic neuritis is an inflammation of the optic nerve (II) in any part of its course When it occurs behind the eyeball it is a *retrobulbar neuritis* when it occurs in the papilla it is a *papillitis* Optic neuritis is of frequent occurrence It arises from multiple etiologic factors and is of grave significance since it may terminate in loss of vision

Classification —Inflammations of the optic nerves may result from damage to *extraneural elements* of the media of the eye or to *neural factors* involving optic nerve optic chiasm optic tract primary visual end stations in the thalamus optic radiation or calcarine cortex

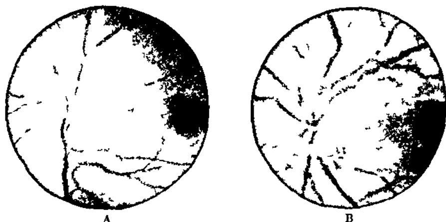


Fig 396 —*A* Postneuritic atrophy *B* Optic neuritis

Axial Optic Neuritis —Axial optic neuritis is usually of the retrobulbar variety The inflammation may be acute or chronic and occurs most often in young females The onset is announced by sudden cloudiness or dimness of vision frontal headache and orbital pain which is increased by pressure on or movement of the eyeballs

Examination reveals *mydriasis* and a *central visual defect* or *scotoma* The fundus appears hyperemic and there may be some blurring and swelling of the disk Progression of the lesion leads to *optic atrophy* with *temporal pallor* which may be unilateral or bilateral Retrobulbar neuritis is seen most often in multiple sclerosis (p 1504) and with nasal sinusitis (p 2124)

Leber's Atrophy —A hereditary axial neuritis affecting males and transmitted by unaffected females (Leber s atrophy) is characterized by an increasing *central scotoma* which affects *color vision* before it involves form *Nyctalopia* (*night blindness*) is a common symptom and total blindness occurs in almost one third of those who are affected The appearance of the fundus is that of an *optic atrophy* most marked temporally

Intra ocular Optic Neuritis or Papillitis —Papillitis is initiated by sudden and marked peripheral contraction of the fields of vision although there

* Gifford, Textbook of Ophthalmology

may be a central scotoma Impairment of vision may precede ophthalmoscopic findings which consist of redness and swelling of the disk blurring of disk margins dilatation of veins narrowing of arteries and sometimes hemorrhage and exudate Recovery may be complete but there is generally some degree of post neuritic or secondary atrophy marked by a dirty gray white appearance of the nerve head filling in of the physiological cup and sheathing of blood vessels (perivasculitis) Papillitis is often confused with *papilledema* (p 1577) and pseudoneuritis (p 1564) The marked loss of vision with sudden onset and a central scotoma generally distinguishes the condition from papilledema The degree of swelling is also less rarely exceeding 2 diopters *Pseudoneuritis* is differentiated by the absence of venous engorgement hemorrhages or exudates the normal sized blind spot and the fact that the condition is non progressive

Diffuse Optic Neuritis—Involvement of the entire optic nerve is often associated with a variety of *infections* which include influenza syphilis scarlet fever malaria yellow fever erysipelas and epidemic encephalitis The severity is such that the amblyopia is accompanied by a *papilledema* that may reach 4 or 5 diopters of swelling

Etiology—The causes of optic neuritis are as varied as the clinical manifestations They differ according to the site of the disturbance

- Extraneural Factors
  - Primary Retinitis
  - Retinitis Pigmentosa
  - Secondary Retinitis
    - Albuminuric
    - Syphilitic
    - Degenerative as in Amaurotic Family Idiocy
- Neural Factors
  - Peripheral due to local injury or disease involving the nerve within the orbit or as far back as the optic chiasm
    - Fracture of Base of Skull
    - Orbital Neoplasm
    - Neoplasm of Orbital Gyrus or Frontal Lobe
    - Gliomas of Optic Nerve
    - Neurofibromas of Optic Sheath
    - Periostitis of Walls of Optic Foramen
  - Orbital Cellulitis secondary to infections of eyelid or nasal accessory sinuses (sphenoid and ethmoid)
- The Optic Chiasm
  - Lesions of the Hypophysis
  - Involvement of the Sella Turcica
  - Sphenoid Sinusitis
- The Optic Tract
  - Cerebrovascular Disease
  - Neoplasms of the Base of the Skull
  - Localized Meningitis
- The Primary Visual End Station
  - Inflammations of lateral geniculate bodies or the pulvinar of the thalamus (vascular or neoplastic)
- The Optic Radiation
  - Vascular Disease Inflammation or Neoplasm of the Occipital Lobe
- The Calcarine Cortex
  - Degenerative Sclerotic Inflammatory Neoplastic or Vascular Disorders of the Occipital Lobes

Clinical Manifestations—The clinical manifestations of optic neuritis consist of subjective complaints evidences of defects in the visual field and abnormalities noted by ophthalmoscopic examination

Subjective Complaints—The patient may complain of clouding of vision frontal headaches orbital pain day blindness night blindness (nyctalopia), field defects, or visual perversions such as red vision (erythropsia) after cataract extraction and yellow vision (xanthopsia) after the excessive use of santonin (p 1896) or digitalis (p 860)

Visual Field Defects—In an *axial neuritis* the field defects are central with retention of peripheral vision Often the disturbance is first apparent with color rather than black and white By contrast there is a concentric field defect in the *intra ocular types of neuritis* with preserva

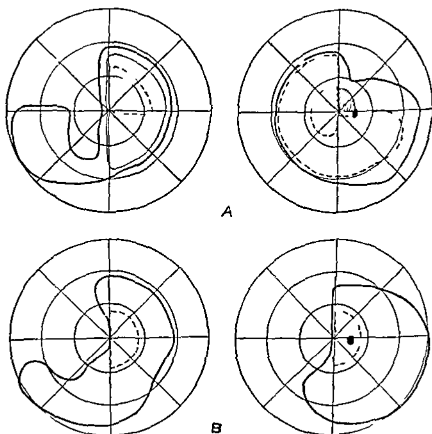


Fig 397—*A* Bitemporal hemianopia Different phases shown by quantitative testing *B* Homonymous hemianopia incongruous *

tion of central vision The more ominous *diffuse neuritis* causes a complete amblyopia or blindness

The visual disturbances serve also to localize the site of the defect from before backward *Unilateral blindness* follows destruction of a single peripheral area A lesion of the central portion of the optic chiasm produces loss of function in the nasal halves of both eyes (*bitemporal hemianopsia*) most often seen in hypophyseal neoplasms (p 1175) This lesion is known also as a *heteronymous hemianopsia* Lesions behind the chiasm produce a *homonymous hemianopsia* in which the field defect involves the

* Traquair in Berens The Eye and Its Diseases

ipsilateral nasal half and the *contralateral temporal portion* The production of a *binasal hemianopsia* requires the operation of two separate lesions involving the lateral portions of the chiasm and is all but unknown *Quadrantic hemianopsias* detectable only by tangent screen examinations arise with lesions of the temporal lobe involving temporal portions of the optic radiation the cuneate lobule above the calcarine fissure or the lingual gyrus

Ophthalmoscopy—Examination with the ophthalmoscope reveals redness blurring and swelling of the disk in an active peripheral neuritis The

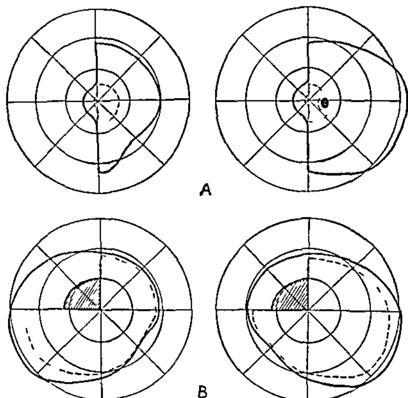


Fig 328—*A* Homonymous hemianopia congruous with macular sparing enlargement of blind spot *B* Homonymous hemianopic quadrant scotomas

retrobulbar types are characterized by pallor particularly in the temporal halves as illustrated in multiple sclerosis tabes and poisonings with alcohol and tobacco With *secondary optic atrophies* the lamina cribrosa which normally is visible in the central cup disappears entirely as opposed to the appearance in the primary atrophy where it can be seen up to the edge of the disk (Fig 326)

Beside the changes in the disk varying degrees of *papilledema* may be observed even in the absence of increased intracranial pressure (p 1468) the veins are engorged the presence of *retinal hemorrhages* suggests vas

T aquair in Berens The Eye and Its D seases

cular disease or a hemorrhagic diathesis *copper wire arteries* which compress the veins indicate a hypertension or advanced arteriosclerotic disease *albuminuric deposits* are observed in nephritis (p 2362) *pigmentations* are present in certain types of retinitis *choroid tubercles* are of ominous diagnostic significance as is the *cherry red spot* in the macula (p 1584)

Diagnosis —The gravity of an optic neuritis constitutes an urgent indication for *specialist consultation* The ophthalmologist is requested to map out with exactitude the *local ophthalmological findings* *Rhinological* and *radiographical surveys* are required with particular reference to the sphenoids and ethmoids since prompt operative interference may save vision if the neuritis is due to inflammation of these structures The *neurological* status is defined by the neurologist or neurosurgeon

In concert with the specialist consultants the practitioner inquires into the uses of *poisons* and *drugs* such as nicotine lead methyl alcohol quinine and the arsenics particularly tryparsamide he seeks evidence of *metabolic disorders* including avitaminoses (p 616) diabetes mellitus (p 1246) or renal insufficiency (p 2362) A *blood serological test* is done for syphilis and spinal fluid is collected after manometric measurements *Radiographs* of the skull may reveal evidences of fracture of spheno-ethmoiditis (p 2125) or increased intracranial tension (p 1468) the *hemogram* reflects the disturbances that characterize the hemorrhagic diatheses (p 3704)

Other *neurological phenomena* are encountered in the widespread afflictions of the nervous system such as multiple sclerosis (p 1504) tabes dorsalis (p 1464) general paresis (p 1377) Friedreich s or Marie s ataxia and the reticulo endothelioses particularly amaurotic family idiocy and Niemann Pick s disease (p 1134)

Treatment —The treatment of the optic neuritis depends upon the causative phenomenon The best results are seen when poisons or causative drugs can be eliminated with the correction of metabolic disturbances following operative interference in sphenoid ethmoiditis (p 2126) after the removal of a brain tumor and vigorous specific therapy of syphilis (p 340) combining massive doses of penicillin and hyperpyrexia

OPTIC ATROPHY

Primary optic atrophy consists of atrophy of the nerve without gliosis caused by a nonvisible lesion The nerve head becomes pale and details of the cribriform lamina become visible ophthalmoscopically *Secondary* optic atrophy results from preceding visible disease usually papilledema or neuritis There is gliosis of the optic disk filling in the physiological cup and blurring the margins The vessels diminish in caliber in severe cases and vision is reduced depending on the severity of the process

The *diagnosis* and *treatment* of optic atrophy are more fully discussed in the sections on optic neuritis (p 1640) and papilledema (p 1577 1579)

OPHTHALMOPLEGIA

Ophthalmoplegia may result from the single or combined involvement of the *third fourth* and *sixth cranial nerves* *External* ophthalmoplegia involves the movements of the eyeball alone in *internal* ophthalmoplegia

the iris and ciliary body are involved *total* ophthalmoplegia embraces both varieties Table 112 names the muscles of the pupil and those which control extra ocular movement defines their normal function and gives the symptoms of deficient action (p 1646)

DIFFERENTIAL DIAGNOSIS OF

Disturbances of the Fields of Vision

With disturbances of the fields of vision the patient requires reference to the consultant ophthalmologist as well as the neurosurgeon The implications are serious and operative intervention may be contemplated

	DIAGNOSTIC FEATURES
Homonymous Hemianopsia (Blindness of Corresponding Lateral Halves of Visual Fields)	From lesion above optic chiasm Cerebral neoplasms except for tumors of third ventricle Cerebral thrombosis involving posterior occipital artery Cerebral embolism or hemorrhage Migraine *Aneurysm of internal carotid artery*
Heteronymous Binasal Hemianopsia	Rarely observed
Heteronymous Bitemporal Hemianopsia	Lesion of central portion of optic chiasm located anterioposteriorly Tumors of pituitary gland or third ventricle Brain abscess Cerebrospinal syphilis with positive serology and spinal fluid findings (p 3734) Acromegaly with deformities of sella turcica
Vertical Hemianopsia	Rarely observed
Concentric or Irregular Contractions of Visual Fields	Optic neuritis and atrophy with demonstrable fundus changes (p 1640) Hysteria without demonstrable organic findings Retinitis exudative choroiditis detachment of retina or retinal hemorrhages observed by ophthalmoscopy (p 1634) Opacity of cornea with changes noted by slit lamp (p 1544) Glaucoma with increased intracranial tension Multiple sclerosis with intention tremor scanning speech and other neurologic manifestations Poisoning with wood alcohol or quinine
Scotomas (Muscae Volitantes and Blind Spots)	May accompany any abnormality of the visual apparatus Also seen without organic ocular findings in migraine anemias leukemia, thrombocytopenic purpuras poisonings alcoholism, auto-intoxication, eye strain and the neuroses

Oculomotor Neuritis —Inflammations of the oculomotor nerve (III) whether or not accompanied by trochlear involvement are manifested by *ptosis diplopia strabismus* and *pupillary changes*

Etiology —Oculomotor neuritis may result from *nuclear lesions* which follow an acute infection such as measles scarlet fever chickenpox small pox influenza epidemic encephalitis acute anterior polio-encephalitis or

TABLE 112—FUNCTIONS AND INNERVATIONS OF MUSCLES OF THE EYES AND FACE AND SYMPTOMS OF DEFICIENT ACTION

Muscle	Normal Function	Symptoms of Deficient Action	Innervation
Ciliary	Makes lens more convex aids in accommodation	Loss of accommodation spasm of ciliary muscle may cause myopia	The third nerve
Sphincter iridis	Contracts pupil to light and during accommodation	Paralytic mydriasis no contraction to light and during convergence or accommodation	The third nerve
Dilator pupillae	Dilates pupils	Pupil does not respond to sensory stimulation	Sympathetic
Rectus superior	Moves eye upward and inward acts with inferior oblique	Upward movement limited diplopia false image above deficiency in rotation of eyeball	The third nerve
Rectus inferior	Moves eye downward and rotates it inward acts with superior oblique	Imperfect movement downward eye rotated outward	The third nerve
Rectus internus	Moves eye inward	Strabismus divergens defective inward pull	The third nerve
Obliquus inferior	Acts with rectus superior moves eye upward and outward rotates it upward	Imperfect movement upward eye rotated inward	The third nerve
Obliquus superior	Moves eye downward and outward acts *with inferior rectus rotates downward*	On looking downward eye is pulled inward convergent strabismus diplopia on stepping downward	The fourth nerve (trochlearis)
Rectus externus	Moves eye outward	Outward movement impaired head turned in direction of paralyzed muscle	The sixth nerve (abducens)
Levator palpebrae superioris	Raises upper eyelid	Ptosis eye closed may be opened a little by frontalis muscle	The third nerve

cervicospinal meningitis in association with cerebrospinal syphilis in the various scleroses of the voluntary nervous system (p 1502) with vitamin deficiencies (hemorrhagic polio-encephalitis of Wernicke) in cerebrovascular disease particularly with involvement of the pyramidal tract in myasthenia gravis hyperthyroidism and migraine (*ophthalmoplegic migraine* (p 1506))

The *efferent nerve* may be involved in its passage through the meningeal envelopes of the brain in acute and chronic *meningeal infections* and *suppurative processes* that involve the cranial bones Peripheral palsies may be *toxic* due to diphtheria rheumatic fever pneumonia diabetes and poisonings by nicotine lead and alcohol Occasionally they are produced by *fractures of the base of the skull* or they become involved in an *aneurysmal dilatation* of the vessels of the circle of Willis (p 968)

Clinical Manifestations—The manifestations of oculomotor paralysis are dependent on the site of the lesion Disease of the *ciliary ganglion* gives rise to *internal ophthalmoplegia* in which there is paralysis of the



Fig 329—Paralysis of left superior oblique

phincter iridis and the ciliary muscles with loss of the reactions to light accommodation and convergence Complete involvement of the *nucleus* or the *efferent portion of the third nerve* results in *complete internal ophthalmoplegia* in which the eye is turned outward the upper lid droops and responses to light and convergence are lost Each of these syndromes differs from the *Argyll Robertson pupil* which is miotic irregular unresponsive to light but reactive to accommodation

Trochlear Neuritis—Lesions of the efferent portion or the nucleus of the *fourth nerve* are relatively rare and difficult of demonstration They are suspected when the patient complains of *double vision* on going down stairs The condition is so unusual that it requires specialist investigation

Abducens Neuritis—Neuritis of the *sixth nerve* whether nuclear or peripheral produces an *internal strabismus* A common cause for an isolated sixth nerve paralysis is involvement by an osteomyelitis of the petrous pyramid secondary to infections of the ear (Fig 330) The resultant

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Gradenigo s syndrome consists of the combination of otogenic infection and internal strabismus

Diagnosis —The presence of an ophthalmoplegia calls for a complete diagnostic survey The blood and spinal fluids are examined with particular reference to the presence of *syphilis* With sixth nerve paralysis an *otological consultation* is warranted for evidence of suppuration in the *petrous bone* (p 2894) Evidences of endogenous metabolic conditions such as *diabetes mellitus* and *nephritis* are sought and the history of vitamin deficiency or exposure to *chemicals drugs and intoxicants* is carefully noted Radiographs of the skull are taken for evidences of *fracture* or *increased intracranial pressure*

When all of the data have been obtained a *neurological consultation* is warranted to correlate the evidence and arrange a plan of therapy



Fig 330—Right congenital abducens paralysis with retraction syndrome *A* Eyes to right Right eye remains in midline *B* Eyes to left Right eye shows retraction and narrowed palpebral fissure in adduction *

Treatment —The treatment of an ophthalmoplegia depends upon the underlying cause Best results are obtained by *antisyphilitic treatment* in lues and by elimination of the effects of endogenous and exogenous poisonings The ophthalmoplegia of *migraine* (p 1506) disappears when the attack is terminated

ALLERGY

The ophthalmological atopies include *allergic* and *vernal conjunctivitis* and *phlyctenular keratoconjunctivitis* There is a suggestion that *uveitis* and *keratitis* secondary to focal infection may be *bacterial allergies* (p 547)

Allergic Conjunctivitis —Conjunctival inflammation in susceptible patients may result from exposure to a number of allergens such as pollens bacterial proteins vegetable proteins animal dust house dust serums foods chemicals locally applied drugs cosmetics and dyes

* Gifford Textbook of Ophthalmology

In conjunctival allergy the membrane appears boggy and edematous and there is a mucoid or mucopurulent discharge The predominant symp

DIFFERENTIAL DIAGNOSIS OF

Ptosis

Drooping of the upper lid may result from muscle weakness or oculomotor palsy which may be induced centrally or peripherally

	DIAGNOSTIC FEATURES
Congenital	Usually bilateral (p 1562)
Physiologic	Transitory with fatigue
Functional	Transitory in neuroses hysteria and ophthalmoplegic migraine
Poisonings	With carbon monoxide sulfonal and lead
Myopathies	Myasthenia gravis with therapeutic response to neostigmine (p 2886) Progressive muscular atrophies
Metabolic	Diabetes mellitus with hyperglycemia and glycosuria Hyperthyroidism with marked exophthalmos elevation of B M R and therapeutic response to iodide Vitamin deficiencies with therapeutic response to thiamine and niacin Schuller Hand Christian disease of children with diabetes insipidus and bone infiltrations
Infections of Central Nervous System	Tabes dorsalis general paresis and syphilitic meningitis with positive serology and characteristic changes in cerebrospinal fluid Meningococcic tuberculous and other types of meningitis with demonstrable pathogenic organisms in cerebrospinal fluid The encephalitides and acute anterior poliomyelitis with other neurologic findings and changes in cerebrospinal fluid Diphtheria with ulceromembranous infection and demonstrable organisms by spread and culture
Peripheral Neuropathies	With facial palsies
Central Neuropathies	Tumor of corpora quadrigemina (bilateral ptosis and sluggish or absent pupillary reflexes) Tumor of pons (ipsolateral oculomotor palsy with contralateral rhythmic tremor) Tumor of crura (ipsolateral oculomotor paralysis and and contra lateral hemiplegia) Tumor of cerebellopontine angle with vertigo deafness and papilledema Refer to neurosurgeon
Disturbances of Involuntary Nervous System	Paralysis of superior cervical ganglion causing enophthalmos and miosis
Descriptive Neuropathies	Multiple sclerosis with disseminated neurologic lesions scanning speech intention tremor and nystagmus (p 1502)

tom is *itching* which may be intractable The diagnosis is established by the demonstration of numerous *eosinophils* in smears and epithelial scrapings

Conjunctivitis Due to Hay Fever—Conjunctivitis is a usual accompaniment of *hay fever* (p 2097) Adults may complain only of pruritus and tearing but children suffer severe inflammation Palliation is afforded by dark glasses frequent irrigations applications of cold compresses and instillations of mildly astringent drops Pyribenzamine (p 565) in 50 mg doses four times daily gives promise of striking symptomatic relief

Phlyctenular Keratoconjunctivitis—Phlyctenular keratoconjunctivitis also known as *eczematous keratoconjunctivitis* is characterized by the presence of circumscribed pinkish white nodules on the cornea and on the bulbar conjunctiva near the limbus The lesions consist of accumulations of lymphoid cells which soften and ulcerate Symptoms vary from mild itching to the most intense lacrimation photophobia and blepharospasm Healing of the lesion is usually complete but repeated crops of corneal phlyctenules result in a marked pannus or vascularization of the cornea and permanent opacification

Etiology—Phlyctenules represent an atopic reaction of the hypersensitive cornea and conjunctiva to an allergen The latter is usually bacterial and more specifically is most often a *tuberculoprotein* (p 259)



Fig 331—Vernal conjunctivitis *A* Palpebral type *B* Limbar type

Treatment—If corneal involvement is present specialist consultation is sought Local treatment includes the uses of 1 per cent yellow oxide of mercury ointment anesthetic drops with epinephrine hot compresses and dark glasses *Specific treatment* includes a thorough search for and the removal of foci of infection (p 42) On indication tuberculin therapy is instituted (p 1551)

Pyribenzamine (p 565) in 50 mg doses four times daily gives promise of striking symptomatic relief

VERNAL CONJUNCTIVITIS OR CATARRH

Vernal conjunctivitis occurs in children around the age of puberty It gradually becomes less severe each successive summer until after a number of years it disappears It is probably an *allergic conjunctivitis* due to dust and aggravated by dry heat The condition is common in the United States Symptoms occur only in warm weather and disappear in the win

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ter although objective evidences of the disease may be present throughout the year

The patient complains of severe itching tearing and photophobia In the *palpebral type* of the disease hard flat papillae are seen on the upper lid giving a cobblestone appearance In less marked cases the conjunctiva appears silky has a bluish white color and is covered by a fine film of stringy secretion which contains eosinophils In the *bulbar form* small yellowish elevations occur at the limbus (Fig 331) This type is most generally seen in Negroes An occasional corneal ulcer may occur

Treatment —Local treatment consists of the use of ice compresses the wearing of dark glasses and instillations of anesthetic drops containing epinephrine (p 1548) Tripbenzamine (p 565) in 50 mg doses four times daily gives promise of striking symptomatic relief

SI CTION \II

THE DIGESTIVE SYSTEM

Associate Editor for Material on the Oropharynx LEO STERN D D S

CHAPTER 81

THE OROPHARYNX INTRODUCTION METHODS OF DIAGNOSIS AND TREATMENT

ANATOMY

The structures of the oropharynx include the *lips vestibule of mouth oral cavity buccal mucous membrane teeth and gums tongue palate pharynx* and *salivary glands* The tonsils and lymphoid tissues of the nasopharynx are discussed with the respiratory system since the management of disturbances of these structures is the province of the rhinologist (p 2021)

While the oropharynx is essentially the realm of the dental surgeon the practitioner often obtains valuable information from a survey of the mouth and its integral parts as exemplified in the tables devoted to the local manifestations of systemic disease (p 1667)

PHYSIOLOGY

Mastication —Mastication is accomplished by grinding food between the teeth of maxilla and mandible after the reception of food the wedge-shaped anterior teeth shear off a morsel by a simple upward thrust of the mandible the bolus is transferred to and balanced between the posterior teeth through the activities of lips cheeks and tongue Here the sidewise movements of the mandible enable the millstone-shaped biting *surfaces* to divide the food mass into a size suitable for swallowing

Salivary Digestion —Salivary secretion appropriate to the character and requirements of the bolus of food is stimulated by masticatory movements and by conditioned and unconditioned reflexes which are mechanically and chemically initiated The secretion of the *submaxillary gland* is thick and viscid while that of the *parotid gland* is serous and contains amylase (ptyalin) saliva lubricates and softens the bolus dissolves water-soluble constituents of food and begins starch digestion

Mastication initiates *gastric digestion* food is crushed in such manner as to release flavors and odors that stimulate nerve endings in palate cheeks lips tongue and olfactory epithelium These agreeable stimuli promote the flow of digestive juices

SPECIAL METHODS OF INVESTIGATING DISTURBANCES OF THE OROPHARYNX

Examination by the Practitioner—The routine examination of the oropharynx (p 3599) should be carried out with great care Pathologic changes in the oral cavity are intimately related to many of the disturbances of *metabolism* and *digestion* to *systemic infections* and disorders of the *blood* and *blood forming structures*

Intra oral examination should follow an orderly plan if errors of omis sion are to be avoided After noting the *odor of the breath* (p 1660) lips vestibule and buccal mucosa are inspected With mouth opened the hard and soft palate dorsal and ventral surfaces of the tongue floor of mouth and exposed surfaces of teeth are scrutinized

Dentures are removed and inspected after which the jaws are closed to observe the interlocking relationship of the remaining teeth Notation is made concerning *missing* or *carious teeth* and the presence of *erosive cavities* and *malpositions tenderness* is sought by applying pressure to or tapping individual teeth, *recession of gums* and *gingival exudate* are espe cially significant the presence of any *eruption pigmentation swelling* or *tumor* requires further investigation an *abnormal mass* (p 1714) or *large ulcer* (p 3600) is palpated using a finger cot or glove for the protection of the examiner The protected finger is introduced into the mouth while extraoral palpation is accomplished through the floor of the mouth and the submandibular region or cheek

Local examination is concluded by palpation of the *lymph nodes* in the parotid sublingual submaxillary infra auricular and anterior cervical regions

Laboratory Aids to Oral Investigation—Laboratory examinations are of limited value to the practitioner in his investigation of the oropharynx *gingival exudate* is stained with dilute carbolfuchsin in the case of ulcero membranous lesions suggesting fusospirochetal infection (p 355), hemor rhagic oral manifestations call for a hemogram (p 1676) since hematopoi etic diseases and leukemias often display their first manifestations on the buccal mucosa On rare occasions the smear reveals a *fungus* the *diph theria bacillus* or *actinomyces Cultures* obtained by aseptic technic from a tooth socket or the root of an extracted tooth may yield a growth of mouth saprophytes or of pathogens intimately concerned with the de ranged process

An indurated ulcer arouses the suspicion of primary syphilis *darkfield examination* (p 45) may reveal spirochetes many weeks before the *com plement fixation test* (p 334) becomes positive

The Dentist and the Oral Surgeon—The dentist and oral surgeon are en titled to close cooperation from the practitioner patients are encouraged to visit these specialists at regular intervals for special examinations and treatment

Inspection Transillumination and Vitality Tests—The dentist notes the presence of caries and erosive cavities transillumination of the gum area is of limited value when x rays cannot be obtained vitality of the dental pulp is tested by its response to a faradic current

Biopsy—Biopsies are made of any tumor or nonfluctuant swelling of soft parts The field of dental pathology is so specialized that expert

opinion should be obtained particularly relative to malignancy In suspected cysts the diagnosis may be verified by aspiration and examination of the fluid

Dentures and Nerve Blocks—In the investigation of pain the removal of a denture sometimes affords relief of the discomfort thus furnishing a simple solution to an otherwise difficult problem Localization of an in

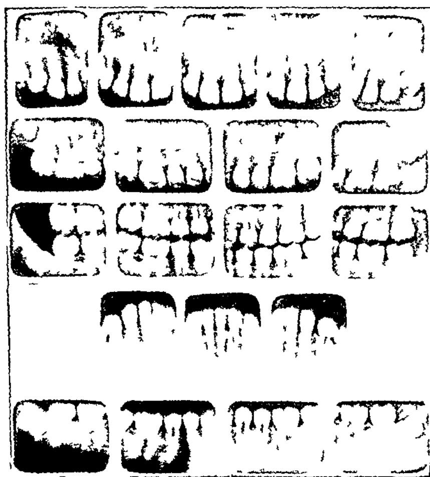


Fig 339—Twenty film intra-oral roentgenographic survey for adult Sixteen periapical and 4 bite wing views

volved nerve segment in neuralgia may be accomplished by injecting procaine at appropriate nerve foramina

Dental X-rays—Dental x rays are easily made but rarely conform to required standards The roentgenograms should be made in such fashion as to present two undistorted angulations of each tooth and the edentulous areas This survey generally requires fourteen or more pictures

A comprehensive interpretation of dental x rays includes enumeration

McCall and Wald Clinical Dental Roentgenology

of *pulpless teeth* with notes concerning the status of the surrounding *peri apical bone* *Unerupted* or *impacted teeth* *alveolar bone destruction* and unusual areas of *radiotranslucency* are described The significance of ab normalities should be estimated by the dentist in terms of dental infec tion Appraisal of the possible relationship between oral condition and systemic manifestations is the province of the practitioner particularly since many dentists exaggerate the importance of focal infection of dental origin

Sialography —Radiography after instillation of an opaque medium into the salivary ducts permits interpretation of the roentgenograms by sialog raphy

SPECIAL METHODS OF TREATMENT IN DISORDERS OF THE OROPHARYNX

Hygiene of the Mouth —The care of the mouth is essential for protection of teeth and for proper initiation of digestive processes Of living organ



Fig 333 —Sixteen film intra-oral roentgenographic survey for child Twelve periapical and 4 bite wing views (child films) *

isms man alone employs *artificial methods of cleansing the mouth* In other animals the activity of tongue lips oral and salivary secretions seems adequate to maintain the integrity of mucous membranes and teeth It is generally believed that the effete and soft diet of civilized man con tributes to dental decay and the vulnerability of the gums

The integrity of diverse metabolic and hematologic factors is essential to the health of the mouth Calcium and vitamin D are important in the development of the *enamel substance* (p 3597) vitamin A contributes to *the formation of dentin,* vitamin C and the formed elements of the blood are necessary for the integrity of the *gums*

In the Newborn —The newborn child is given water to drink follow ing milk feedings so that the mouth is rinsed gums are kept soft and clean by a mild *alkaline wash* applied with a soft cloth or a cotton ap-

* McCall and Wald Clinical Dental Roentgenology

plicator The administration of vitamins A and D may improve the qual ity of tooth formation

The teeth of the infant are cleansed with a weak solution of *soap* Children are taught to brush the teeth and rinse the mouth after each feeding

Dental Prophylaxis in the Normal Adult—Despite all efforts at adequate mouth hygiene tartar deposits between the teeth and along the gingival margin make it essential for the patient to visit dentist or dental hygienist two or three times annually At this time cavities are easily filled and extensive dental decay and infection are effectually prevented

Dental prophylaxis consists of removal of *deposits of tartar* from the necks of the teeth and cleansing of dental surfaces It is recommended as a routine procedure in health as a pre anesthetic precaution and to re

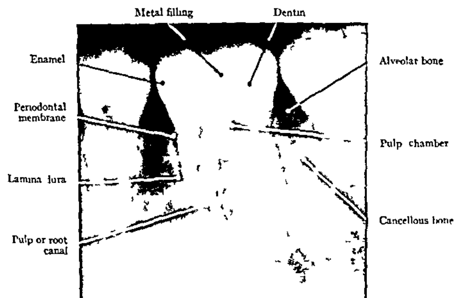


Fig 334—Enlarged roentgen gram of the lower right side in an adolescent showing normal dental and periodontal structures

store oral health after illness Removal of deposits from beneath the gum margins eradication of recesses that serve as bacterial incubation zones and adjustments of the bite are essential to the final cure of any type of *periodontoclasia* (p 1700)

Oral Hygiene in Pregnancy and Illness—The care of the mouth is of particular importance during prolonged illness and pregnancy The gravid woman should protect her teeth by careful local hygiene and for the benefit of the fetal dental structure should consume adequate amounts of *calcium* and *vitamin D*

During severe illness the care of the mouth is usually delegated to the attendant or the nurse The patient is encouraged to stimulate salivary secretion by *rinsing the mouth* and by *chewing gum* the mucous mem

McCall and Wald Clinical Dental Roentgenology

of *pulpless teeth* with notes concerning the status of the surrounding *periapical bone* *Unerupted* or *impacted teeth* *alveolar bone destruction* and unusual areas of *radiotranslucency* are described The significance of abnormalities should be estimated by the dentist in terms of dental infection Appraisal of the possible relationship between oral condition and systemic manifestations is the province of the practitioner particularly since many dentists exaggerate the importance of focal infection of dental origin

Sialography —Radiography after instillation of an opaque medium into the salivary ducts permits interpretation of the roentgenograms by sialography

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The integrity of diverse metabolic and hematologic factors is essential to the health of the mouth Calcium and vitamin D are important in the development of the *enamel substance* (p 3597) vitamin A contributes to the formation of *dentin*, vitamin C and the formed elements of the blood are necessary for the integrity of the *gums*

In the Newborn —The newborn child is given water to drink following milk feedings so that the mouth is rinsed gums are kept soft and clean by a mild *alkaline wash* applied with a soft cloth or a cotton ap

* McCall and Wald Clinical Dental Roentgenology

Proprietary Mouth Washes—Most proprietary mouth washes are extravagant in claims and price they differ very little from simpler preparations except that they contain a weak deodorant, such as 1 4000 potassium permanganate or a mild astringent such as zinc chloride The most important commercial ingredients of the mouth wash are flavor and coloring matters The flavor is obtained by the addition of mixtures of volatile agents such as thymol menthol peppermint wintergreen cinnamon or clove

Proprietary *alkaline* mouth washes are advertised to combat the oral acidity claimed to favor dental decay if oral hyperacidity were a factor it is difficult to understand how any significant alteration in reaction could result from the occasional use of a weakly alkaline solution

Deodorant Mouth Washes and Halitosis—One of the first and most successful advertising campaigns based on fear was that which stressed offensive odor of the breath Idiopathic halitosis is a clinical rarity when the breath is foul it is commonly the result of some digestive disorder chronic sinusitis ozena putrid gingivitis dental decay the aftermath of the ingestion of odoriferous food such as garlic or decomposition of food particles lodged between the teeth

A time honored deodorant mouth wash is *Dobell s solution*

Phenol	1 0
Sodium Bicarbonate	3 0
Sodium Borate	3 0
Glycerin	10 0
Water q s a d	200 0
Sig Mouth Wash	

The most effectual oral deodorant is a weak solution of *chloramine*

During sickness the mouth is kept properly cleansed by applying a noncaustic iodine preparation to the gums with a cotton swab or applicator A useful prescription for this purpose is

Iodine	1 0
Potass um Iod de	3 0
Glycerin q s a d	30 0
Sig Local Use	

Dentifrices—Dentifrices are universally employed most adults brushing the teeth on arising and when retiring

The most important element of dental hygiene is the correct use of the tooth brush A good stiff brush is essential the main purpose of brushing teeth being to dislodge foreign particles and foodstuffs caught between them The lower teeth should be brushed upwards and the upper teeth brushed downwards in order to prevent irritation of the gum margin and yet effectually reach the interdental spaces The type of *dentifrice* is of minor and accessory importance a weak solution of soap or the salt and sodium bicarbonate mixture prepared for the mouth wash (p 1660) answers all purposes

Proprietary Dentifrices—Despite their relatively minor role in dental hygiene the advertising mediums have focussed public attention on den

branes and gums are kept soft and sweet by applying an *alkaline or soapy solution* with a soft cloth This is mandatory if the patient is on a continuous intravenous drip failure to encourage salivary secretion may lead to *suppurative parotitis* which often proves fatal

The Mouth Wash —The official aqueous mouth wash is *Liquor Antisepticus N.F* an unnecessarily complex solution A satisfactory and inexpensive aqueous mouth wash is prepared by adding a teaspoonful of *table salt* and a teaspoonful of *bicarbonate of soda* to a pint of tap water a few

DIFFERENTIAL DIAGNOSIS OF

Breath Odors

Odors detected on the breath occasionally provide valuable diagnostic clues for the alert practitioner This axiom is best illustrated in the detection of acidosis with its characteristic sweetness of the breath, and of pulmonary suppuration when a putrid odor is noted.

CAUSE	DIAGNOSTIC FEATURES
Sweet Odor	Acidosis Test urine for acetone and sugar (p 3673)
Aromatic Odor	After alcoholic beverages paraldehyde and volatile anesthetics
Heavy Odor	With constipation, auto-intoxication and cholemia (biliousne s ') Test urine for bile pigments and for indican (p 3685)
Musty Odor	Typhoid fever with positive blood culture or elevation of agglutinin titer Measles and scarlet fever with characteristic exanthems
Garlic Odor	After inge tion of onion, garlic or chives Following administration of arsenicals or bism th
Putrid or Offensive Odor	Retention of pus in nose and nasal accessory sinuses Adenoids Atrophic rhinitis (ozena) Pharyngitis Tonsillitis Diphtheria Dental caries Periodontitis Stomatitis Gingivitis Retention of decayed food particles between teeth or under unclean dentures If no abnormality is detected by local inspection, suspect putrid lung abscess and get chest x ray and consider bronchoscopy (p 2075)
Urinous	Azotemia with retention of nitrogenous products in blood, and impairment of renal function tests
Almond Odor	Cyanide poisoning

drops of peppermint or cinnamon water supply a pleasant flavor Another simple mouth wash is made by diluting 1 part of *hydrogen peroxide* with 3 or 4 parts of warm water immediately following the use of hydrogen peroxide a mild alkaline solution is employed to rinse off the acid froth caused by the liberation of oxygen

A *dilute alcoholic mouth wash* is improvised by adding 1 part of alcohol to 4 or 6 parts of water When the gums are inflamed and spongy a 5 per cent solution of *potassium chlorate* may often have a beneficial effect

Proprietary Mouth Washes—Most proprietary mouth washes are extravagant in claims and price they differ very little from simpler preparations except that they contain a weak deodorant, such as 1 4000 potassium permanganate or a mild astringent such as zinc chloride The most important commercial ingredients of the mouth wash are flavor and coloring matters The flavor is obtained by the addition of mixtures of volatile agents such as thymol menthol peppermint wintergreen cinnamon or clove

Proprietary *alkaline* mouth washes are advertised to combat the oral acidity claimed to favor dental decay if oral hyperacidity were a factor it is difficult to understand how any significant alteration in reaction could result from the occasional use of a weakly alkaline solution

Deodorant Mouth Washes and Halitosis—One of the first and most successful advertising campaigns based on fear was that which stressed offensive odor of the breath Idiopathic halitosis is a clinical rarity when the breath is foul it is commonly the result of some digestive disorder chronic sinusitis ozena putrid gingivitis dental decay the aftermath of the ingestion of odoriferous food such as garlic or decomposition of food particles lodged between the teeth

A time-honored deodorant mouth wash is *Dobell s solution*

Phenol	1 0
Sodium Bicarbonate	3 0
Sodium Borate	3 0
Glycerin	10 0
Water q s a d	200 0
S g Mouth Wash	

The most effectual oral deodorant is a weak solution of *chloramine*

During sickness the mouth is kept properly cleansed by applying a noncaustic iodine preparation to the gums with a cotton swab or applicator A useful prescription for this purpose is

Iodine	1.0
Potassium Iodide	3 0
Glycerin q s a d	30 0
Sig Local Use	

Dentifrices—Dentifrices are universally employed most adults brushing the teeth on arising and when retiring

The most important element of dental hygiene is the correct use of the tooth brush A good stiff brush is essential the main purpose of brushing teeth being to dislodge foreign particles and foodstuffs caught between them The lower teeth should be brushed upwards and the upper teeth brushed downwards in order to prevent irritation of the gum margin and yet effectually reach the interdental spaces The type of *dentifrice* is of minor and accessory importance a weak solution of soap or the salt and sodium bicarbonate mixture prepared for the mouth wash (p 1660) answers all purposes

Proprietary Dentifrices—Despite their relatively minor role in dental hygiene the advertising mediums have focussed public attention on den

branes and gums are kept soft and sweet by applying an *alkaline or soapy solution* with a soft cloth This is mandatory if the patient is on a continuous intravenous drip failure to encourage salivary secretion may lead to *suppurative parotitis* which often proves fatal

The Mouth Wash —The official aqueous mouth wash is *Liquor Antisepticus N.F* an unnecessarily complex solution A satisfactory and inexpensive aqueous mouth wash is prepared by adding a teaspoonful of *table salt* and a teaspoonful of *bicarbonate of soda* to a pint of tap water a few

DIFFERENTIAL DIAGNOSIS OF

Breath Odors

Odors detected on the breath occasionally provide valuable diagnostic clues for the alert practitioner This axiom is best illustrated in the detection of acidosis with its characteristic sweetness of the breath and of pulmonary suppuration when a putrid odor is noted

CAUSE	DIAGNOSTIC FEATURES
Sweet Odor	Acidosis Test urine for acetone and sugar (p 3673)
Aromatic Odor	After alcoholic beverages paraldehyde and volatile anesthetics
Heavy Odor	With constipation auto-intoxication and cholemia (biliou ness) Test urine for bile pigments and for indican (p 3685)
Musty Odor	Typhoid fever with positive blood culture or elevation of agglutinin titer Measles and scarlet fever with characteristic exanthems
Garlic Odor	After ingestion of onion, garlic or chives Following administration of arsenicals or bismuth
Putrid or Offensive Odor	Retention of pus in nose and nasal accessory sinuses Adenoids Atrophic rhinitis (ozena) Pharyngitis Tonsillitis Diphtheria Dental caries Periodontitis Stomatitis Gingivitis Retention of decayed food particles between teeth or under unclean dentures If no abnormality is detected by local inspection, suspect putrid lung abscess and get chest x ray and consider bronchoscopy (p 2075)
Urinous	Azotemia with retention of nitrogenous products in blood, and impairment of renal function tests
Almond Odor	Cyanide poi oning

drops of peppermint or cinnamon water supply a pleasant flavor Another simple mouth wash is made by diluting 1 part of *hydrogen peroxide* with 3 or 4 parts of warm water immediately following the use of hydrogen peroxide a mild alkaline solution is employed to rinse off the acid froth caused by the liberation of oxygen

A *dilute alcoholic mouth wash* is improvised by adding 1 part of alcohol to 4 or 6 parts of water When the gums are inflamed and spongy a 5 per cent solution of *potassium chlorate* may often have a beneficial effect

Usual untoward sequels to *procaine injection* consist of tachycardia hypertension sweating and trembling These reactions disappear spontaneously within a few minutes More severe symptoms are rare and include syncope and anginal pains Syncope is relieved by postural treatment anginal pains yield to amyl nitrite or glyceryl trinitrate

Mild cardiovascular reactions to *procaine epinephrine solution* occur often and are controlled by reducing the epinephrine concentration to 1 75 000 and by preliminary basal anesthesia (p 3811)

General Anesthesia—The use of general anesthesia in routine oral surgery is to be deprecated The unconscious patient may suffer inhalation of infected material and later develop a *lung abscess* the practitioner occasionally reads of or has the misfortune to experience a sudden *anesthetic death* in the dental chair as the result of idiosyncrasy to the anesthetic gas or of circulatory failure due to stimulation of the carotid pressor receptors

The more commonly used general anesthetics are *nitrous oxide with oxygen vinethene ether* and intravenously administered *pentothal sodium* Dental operations on the unconscious patient should be performed with the pharynx packed with gauze a suction tube is used freely further to reduce aspiratory risk The indications for general anesthesia include extensive oral infection trismus emotional instability on the part of the adult patient and lack of cooperation in childhood

Basal Anesthesia—The principles of basal anesthesia may also be applied to dental surgery by administering double the average dose of a *hypnotic* (p 3913) and/or a subcutaneous injection of morphine or one of its substitutes (p 3853) Ambulatory patients who have received a hypnotic may have to be escorted home

Postoperative Pain—Postoperative dental pain often is severe The physician will save himself and his patients many sleepless nights if he makes available a prescription for a narcotic with an analgesic such as a codein acetylsalicylic acid combination (p 3834)

Fillings—*Dental caries* is treated by complete removal of the decayed tooth structure and replacement by a filling which according to dental criteria must seal the cavity hermetically reproduce the lost anatomy of the tooth and be extended so that its margins are located in zones that are comparatively immune to recurrent decay

Amalgam fillings or *gold inlays* are used in posterior teeth while the less enduring but more pleasingly esthetic *cement acrylic plastic* or *porcelain fillings* are generally favored for anterior teeth

Deep seated fillings are insulated from the dental pulp so as to eliminate thermal or chemical irritation In selected teeth the root canal whose pulp has been exposed or decomposed by the invasion of caries may be treated and filled successfully

Root Amputation—Occasionally a strategically important tooth is cured of periapical infection by surgical *resection of the root apex* The pulpless tooth is vulnerable to infection and reinfection and requires frequent examination

Tooth Extraction—Unequivocal cure of periapical dental infection is accomplished by extraction The practitioner should be consulted by the dentist concerning the choice of anesthetic and contraindications When possible local anesthesia is urged nervous and highstrung individuals

tifrices Most *tooth powders* consist of precipitated chalk with a small amount of soap a sweetening agent (sugar or saccharine) and a flavoring of wintergreen clove violet, thymol menthol or eucalyptol The essential element is the chalk, which has both detergent and polishing properties Too vigorous crosswise brushing with the dentifrice injures teeth and gum margins Tooth powders intended for *stained teeth* contain pumice and cuttle bone which may cause extensive dental and gingival injury Antiseptic tooth powders usually include boric acid salicylic acid salol camphor and essential oils Few therapeutic endeavors match the 'antiseptic tooth powder in the discrepancy between claims and accomplishment *Tooth pastes which enjoy a wide vogue are similar in composition to* powders except that glycerin is added The *liquid* tooth preparations are usually a soap powder or a synthetic detergent with glycerin coloring and flavoring, they are less likely to cause damage than other dentrifices

Dental floss or balsa wood toothpicks carefully used are helpful in dislodging impacted food particles, trauma to the gums must be avoided

Local Applications to the Gums and Teeth —The infected or irritated gum may be treated locally with a variety of preparations

Counterirritant —Oil of Clove Eugenol, Iocamphen Tinctures of Aconite or Iodine

Analgesic —Compound Tincture of Benzoin 3 to 10 per cent Ethyl Aminobenzoate 2 per cent Butyn spray of Ethyl Chloride

Antiseptic and Disinfectant —3.5 per cent Tincture of Iodine 2 per cent Sodium Perborate 1 per cent Acriviolet 1 per cent Gentian Violet

Anti infective Agents —5 per cent Sulfathiazole suspension or Penicillin (1000 units per cc)

Styptic —5 per cent Chromic Acid 5 per cent Potassium Chlorate 8 per cent Zinc Chloride

Caustic —10 to 25 per cent Silver Nitrate 50 per cent Phenol

Amebicide —Fluid extract of Ipecac

Dental Anesthesia —Each practitioner knows from personal experience that successful dentistry requires satisfactory local anesthesia *Most* dental neglect is based upon the justifiable reluctance of the patient to subject himself to pain and discomfort

Topical Applications—Topical applications such as the Hartman s solution (thymol ether and alcohol) and volatile oils have little practical anesthetic value The mucosal surface may be superficially anesthetized by applying 2 per cent butyn (p 3916)

Local Anesthesia—Local anesthesia by infiltration or nerve block affords the greatest relief with the least risk *Infiltration* is advisable for work in the median line or in a localized procedure on a single tooth *nerve block* with or without supplementary local infiltration is more useful when extensive manipulation has to be done in a single field particularly for posterior mandibular teeth

The majority of dentists employ cocaine substitutes such as 2 per cent *procaine* solution with a few drops of 1 1000 *epinephrine* By producing vasoconstriction the latter slows absorption increases the duration and intensity of anesthetic action and diminishes bleeding

ance of excessive traumatism in delivering the tooth and leveling of sharp bony edges of the socket Dislocations of soft tissue are corrected by suture hemorrhage is controlled by gauze packing and infection through autocontamination is prevented by routine application to the wound of powdered sulfanilamide or a penicillin solution

Postoperative Care—Postoperative *dental pain* which is protracted or does not yield to acetylsalicylic acid and codeine may require re dressings of the socket using an analgesic paste of petrolatum and ethyl aminobenzoate *Secondary hemorrhage* is controlled by tight gauze packing supplemented if necessary by Monsel s solution (Liquor Ferri Subsulfatis) In *continued bleeding* a splint of dental wax compound may be applied so as to exert continued pressure *Post extraction swelling* responds to external intermittent application of cold

Impacted Third Molars (*Wisdom Teeth*) —The third molars are the last teeth to be calcified they are not prepared to erupt until the dental arch is virtually formed and the forward growth of the maxillary bones has been completed Often they have insufficient space to erupt and become impacted against the second molars As their eruptive force is retained impacted third molars may continue to exert pressure against sec



Fig 336—*A* Impacted lower third molar *B* Impacted upper left second bicuspid lying buccolingually in close relation to the first molar

ond molars and by contiguity against the entire set of teeth In some patients this is symptomatized by local or reflex pain and in others by migration of the teeth requiring extraction Extraction is often formidable and is not recommended unless the symptoms warrant the hazard

Partially erupted third molars usually lie at an angle of about 45 degrees with the preceding tooth Only the posterior cusps pierce the gum and the pocket formed through breakdown of the unerupted dental follicle may be the site of subacute infection characterized by tenderness swelling and recurrent infection Chronic infections of this type are often residual after oral fusospirochetal invasion and must be completely treated to eliminate an incubation zone which leads to recurrent *Vincent s infection* (p 355)

Orthodontia —Indicated orthodontic treatment contributes to function as well as to appearance Dental disfigurements produce personality changes in hypersensitive individuals

Among wealthier patients orthodontia is too often abused The definitive indications for therapy include those inharmonious arrangements and malocclusions of the teeth which reduce masticating efficiency interfere

McCall and Wald Clinical Dental Roentgenology

should receive the advantage of basal anesthesia patients with hyperthyroidism and cardiovascular disease should be injected with an anesthetic solution containing little or no epinephrine Those who suffer a possible focal infection should have the root of the infected tooth cultured preferably on a blood plate for the preparation of a *vaccine* (p 77)

Indications—Extraction of teeth is indicated to prevent or eradicate local or systemic infection to eliminate teeth which impinge harmfully on adjacent tissues or other teeth to relieve pain and sometimes to rearrange the mouth to conform with the requirements of dental prosthesis

Contraindications—Contraindications to extraction exist when there are coincident physiologic or pathologic states which temporarily consti-



Fig 335—A and *B* Periapical rarefaction of the fibrous type *C* Periapical rarefaction of the diffuse type *D* Periapical rarefaction of the epitheliated type

tute an increased operative hazard Among these are *acute dental infection blood dyscrasias uncontrolled diabetes secondary syphilis* and *cardiovascular crises*

Preoperative Precautions—Hospitalization may be required in handicapped patients or those in whom a difficult extraction is anticipated Immediate pre extraction precautions are directed towards preventing *shock hemorrhage* or *sepsis* Patients with a background of rheumatic fever are given *sulfadiazine* and *penicillin* (p 111) to prevent the onset of subacute bacterial endocarditis (p 1021)

Technic—A satisfactory extraction requires surgical asepsis suitable exposure of the operative field gentle separation of the soft tissues avoid

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CHAPTER 82

CLINICAL DISTURBANCES OF THE OROPHARYNX LOCAL MANIFESTATIONS OF SYSTEMIC DISORDERS

The oropharynx may reveal local manifestations of dermatoses allergy systemic infections endocrine disorders avitaminoses hemorrhagic dia theses and other blood disturbances and poisonings by metals and non metals

ORAL MANIFESTATIONS OF THE DERMATOSES

Eruptions which ordinarily attack the glabrous skin may involve the mucous membranes of lips and mouth The oral lesions may precede the cutaneous eruption or even appear without any exanthem Local treat ment of the mouth lesions is limited to palliative and hygienic measures

Table 113 —Oral Manifestations of the Dermatoses

Erythema M lt forme (p 3374)
In early stages discrete oval ves cles appear on the floor of the mouth the tongue l ps and buccal mucosa after rupture superficial ci cumscribed erosions are produced marked tendency to confluence severe pain w th later ulceration

L p s Erythematos s (p 3399)
Red elevated points on hard palate lips and buccal mucosa coalesce to form irregula ly shaped patches with superficial ulceration ulcers thicken with peripheral redness and central d pression covered with da k exudate healing is slow with residual gray scars of irregular shape recognized by asso ated dermatos s See Fig 337

L h n Pla s (p 3392)
Cluster of pinhead size discrete papules ppears most typically on the buccal mucosa oppo te the biting edges of the posterior teeth lesions are white painless and palpable later become connected by thin interlacing lines so that sharp defin tion is lost less often the eruption appears on the tongue wher t may form plaques recognized by associated d rmatos s See Fig 338

P mph gus (p 340)
Pa less oval bl bs m y appear befo e the cutaneous manifestat ons have occur ed usu ally situated on hard palate gums tongue or lips with rupture of bleb new crop is f rmed until large part of mouth is involved ruptur d blebs leave shallow oval eros ons to wh ch shreds of sl ugh adhere les ons painful and bleed eas ly breath foul as e os ons h al a gray sh pseudomembrane forms recogn ed by assoc ated dermatosis

D matt s He p t fo m s (p 3371)
Small cluster of vesicles appears on the buc al mucosa rupture occurs within a few days leaving dark red ulcers that heal rapidly may be associated with mild burning sensa t on b t rarely severe pa recognized by associated dermatos

with normal facial development and symmetry and increase susceptibility to caries and gingivitis

Treatment should be limited to those abnormalities which are clearly due to postnatal factors such as thumbsucking mouth breathing or rickets it is rarely possible permanently to correct malpositions due to hereditary patterns With rare exceptions interference is advantageously postponed until after the age of twelve since much of the difficulty may be corrected as the jaws grow and expand

Bridges and Dentures (Dental Prosthesis) —Missing teeth if few in number are replaced by dental bridges Fixed bridgework is generally limited to spans which replace one or two teeth Saddles' are added to larger bridges which increase the functional pressure on supporting teeth Bridges provided with saddles must be removable they should be brushed daily with soap and water and immersed in a strong solution of chloramine for fifteen minutes once a week to remove stains encrustations and residual odors

During sleep and prior to anesthesia or intra oral manipulations dentures are removed Ill fitting appliances produce local irritation and ulceration which if continued may lead to malignant change (p 572)

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TABLE 113—ORAL MANIFESTATIONS OF THE DERMATOSES

Erythema Multiforme (p 3374)
In early stages discrete oval vesicles appear on the floor of the mouth the tongue lips and buccal mucosa after rupture superficial circumscribed erosions are produced marked tendency to confluence severe pain with later ulceration

Lupus Erythematosus (p 3399)
Red elevated points on hard palate lips and buccal mucosa coalesce to form irregularly shaped patches with superficial ulceration ulcers thicken with peripheral redness and central depression covered with dark exudate healing is slow with residual gray scars of irregular shape recognized by associated dermatosis See Fig 337

Lichen Planus (p 3392)
Cluster of pinhead size discrete papules appears most typically on the buccal mucosa opposite the biting edges of the posterior teeth lesions are white painless and palpable later become connected by thin interlacing lines so that sharp definition is lost less often the eruption appears on the tongue where it may form plaques recognized by associated dermatosis See Fig 338

Pemphigus (p 3405)
Painless oval blebs may appear before the cutaneous manifestations have occurred usually situated on hard palate gums tongue or lips with rupture of bleb new crop is formed until large part of mouth is involved ruptured blebs leave shallow oval erosions to which shreds of slough adhere lesions painful and bleed easily breath foul as ros o s h l a grayish pseudomembrane forms recognized by associated dermatosis

Dermatitis Herpetiformis (p 3371)
Small cluster of vesicles appears on the buccal mucosa rupture occurs within a few days leaving dark red ulcers that heal rapidly may be associated with mild burning sensation but rarely severe pain recognized by associated dermatosis

DIFFERENTIAL DIAGNOSIS OF

Enanthems Involving Oral and Buccal Surfaces

Eruptions involving oral and buccal mucous membranes may repre ent local proce ses or manife tations of profound sy temic disturbances Recognition of the general characteristic of the individual lesion may enable dentist or practitioner to arrive at a correct diagnosis

	DIAGNOSTIC FEATURES
Erythema	Infectious tomatitis without other manife ta tions Scarlet fever with exanthem and Schultz Charlton *blanching reaction Secondary* syph ilis with positive darkfield findings and serology
Vesicles and Bullae	Infectious stomatitis aphthous stomatitis herpes simplex and herpes zoster without *manifestations elsewhere Contact* dermatitis from cosmetics or dentifrices Dermatitis med icamentosa from drugs Erythema multiforme pemphigus and dermatitis herpetiformis with cutaneous dermatoses Varicella and variola with fever and exanthem Foot and mouth dis ease with extremity lesions
Macules and Papules	Fordyce s condition and leukoplakia without manifestations elsewhere Lichen planus with exanthem Measles with Koplik pots and exanthem
Tumors	Epulis in pregnancy Oropharyngeal cysts with x ray changes and fluid by diagno tic puncture (p 1714) Oropharyngeal neopla ms clarified by biopsy (p 1656) Gummas with posi tive serology and therapeutic response to iodide
Petechiae and Purpuras	Scurvy with therapeutic response to cevitamic acid Vitamin K deficiency with therapeutic response to menadione Leukemias and throm bocytopenic purpura with pathognomonic hemograms (p 3704) Subacute bacterial endo carditis with positive blood culture
Telangiectasis	Hereditary telangiectasis with similar lesions elsewhere and normal hemogram
Ulcers	Aphthous stomatitis without lesions elsewhere *Scurvy with therapeutic response to* cevitamic acid Vitamin B deficiencies with therapeutic re ponse to thiamine riboflavin or niacin Erythema multiforme lupus erythematosus and dermatitis herpetiformis with cutaneous exanthem Ulceromembranous stomatitis or gingivitis with Vincent organisms demon strable on smears (p 50) Epithelioma or car cinoma with positive biopsy Tuberculosis with acid fast organisms demonstrable in exudate or tissue (p 50) Diphtheria with membranous exudate and characteristic organisms in smears and cultures (p 302) Primary or secondary syphilis with positive darkfield and/or ser ology Tertiary syphilis with therapeutic re sponse to iodide Agranulocyto is and leu kemia with characteristic hemogram (p 3704) Typhoid fever with positive blood culture or elevated agglutinin titer (p 60)

TINUED

Pigmentations	Normal deposits in negroes and brunettes Nicotine staining in habitual smokers Depo its of lead and bismuth with positive urine finding (p 3659) Adrenal cortical deficiency with hy potention and asthenia

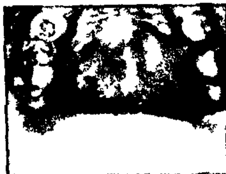


Fig 337—Lupus eryth mato us of palate



F g 338—Lichen planus

ORAL MANIFESTATIONS OF ALLERGY

The structures of the oropharynx may respond as shock organs to local or systemic introductions of an allergen The gums of the adult pa tient who is subject to allergic manifestations are often chronically in flamed and the tissue contains many eosinophiles The diagnosis is sug gested by the history and the effects of elimination of the cause

TABLE 114—ORAL MANIFESTATIONS IN ALLERGY

C tact D mat t s (p 3330)

May be produced by po son ivy c ta n types of lipst ck toothpaste cigarettes c gars pipe stems or food actinic cheil t s re ults from exposu e to sunlight and is often accompanied by a herpes of s m lar origin In severe instances th erupt on may be bullous with ruptu encrustation and heavy scabs in chronic examples the lips be come dry and fissured and assume a lavendar color resembling a cyanos s stomat tis venenata is produced by toothpaste mouthwashes dentures chewing gum and pro caine

Diagnosis from history and results of l m nation of aus

Th ma O al Diagnosis

DIFFERENTIAL DIAGNOSIS OF

Enanthems Involving Oral and Buccal Surfaces

Eruptions involving oral and buccal mucous membranes may represent local processes or manifestations of profound systemic disturbances Recognition of the general characteristic of the individual lesion may enable dentist or practitioner to arrive at a correct diagnosis

	DIAGNOSTIC FEATURES
Erythema	Infectious stomatitis without other manifestations Scarlet fever with exanthem and Schultz Charlton blanching reaction Secondary syphilis with positive darkfield findings and serology
Vesicles and Bullae	Infectious stomatitis aphthous stomatitis herpes simplex and herpes zoster without manifestations elsewhere Contact dermatitis from cosmetics or dentifrices Dermatitis medicamentosa from drugs Erythema multiforme pemphigus and dermatitis herpetiformis with cutaneous dermatoses Varicella and variola with fever and exanthem Foot and mouth disease with extremity lesions
Macules and Papules	Fordyce s condition and leukoplakia without manifestations elsewhere Lichen planus with exanthem Measles with Koplik spots and exanthem
Tumors	Epulis in pregnancy Oropharyngeal cysts with x ray change and fluid by diagnostic puncture (p 1714) Oropharyngeal neoplasms clarified by biopsy (p 1656) Gumma with positive serology and therapeutic response to iodid
Petechiae and Purpuras	Scurvy with therapeutic response to cevitamic acid Vitamin K deficiency with therapeutic response to menadione Leukemias and thrombocytopenic purpura with pathognomonic hemograms (p 3704) Subacute bacterial endocarditis with positive blood culture
Telangiectasis	Hereditary telangiectasis with similar lesions elsewhere and normal hemogram
Ulcers	Aphthous stomatitis without lesions elsewhere Scurvy with therapeutic response to cevitamic acid Vitamin B deficiencies with therapeutic response to thiamine riboflavin or niacin Erythema multiforme lupus erythematosus and dermatitis herpetiformis with cutaneous exanthem Ulceromembranous stomatitis or gingivitis with Vincent organisms demonstrable on smears (p 50) Epithelioma or carcinoma with positive biopsy Tuberculosis with acid fast organisms demonstrable in exudate or tissue (p 50) Diphtheria with membranous exudate and characteristic organisms in smears and cultures (p 302) Primary or secondary syphilis with positive darkfield and/or serology Tertiary syphilis with therapeutic response to iodide Agranulocytosis and leukemia with characteristic hemogram (p 3704) Typhoid fever with positive blood culture or elevated agglutinin titer (p 60)

CONTINUED

TABLE 115—ORAL MANIFESTATIONS OF INFECTION (*Continued*)

Lupus Vulga s (p 3 62)
In lupus vul_aris l ps an l vestibule of mouth involve l oral lesion consists of clusters of superficial soft re l elevations which ulcerate lea ing deep puckered scars on heal ng
Diagnosis by biopsy

Sa co dos s (p 32 1)
Sarcoidosis is a rare manifestat on with s multaneous inflammation of u eal tract and paroti l glands
Diagnosis by b opsy

Erys p las (p 167)
Local zed les on with raised indurated bo der wh ch tends to advance rap dly often associated with severe pain an l constitutional manifestat ons
D agnosis by clinical appearance

He p s S mplex (p 433)
Vesicular lesion of l p (herpes labialis or fe er sore) begins as large hyperemic patch followed by vesicul t on with rupture of vesicle a superf cial eros on forms which becomes covered with a brown crust after shed l ng of en ru tation complete h al ing occurs (See Fig 344)
Pall ative *t eatment*

H rp s Zoster (p 435)
Vesicular les on of l ps cheeks or tongue usually associated with other ves cles along the di tr b it o i of the branches of the fifth nerve e ere pain precedes and a com panies lesion
Pall ative local *t eatm nt*

Foot a d Mouth Di ase (p 437)
Ep demic d sease with ves culation an l pustulat on in oral ca ity an l on feet (See Fig 345)

ORAL MANIFESTATIONS IN ENDOCRINOPATHIES

Early dysfunctions of the endocrine glands may be revealed by the *teeth mandible buccal mucosa* and *tongue* The changes may be corrected or arrested by substitution therapy in deficiencies and by repression of secretion in hyperactivity

TABLE 116 —ORAL MANIFESTATIONS OF ENDOCRINE DISTURBANCES

Hyp thyro d sm (p 1191)
Lips th ck mouth open tongue protrudes ha d palate flat delay in erupt on of teeth malposition and defective tooth stru ture incr ases suscept bility to caries gingivitis and tendency toward sep ation and loo ning of teeth o urs in ad lt myxedema
Therapeut c test with thyro d extract

Hype pa athyro d sm (p 1197)
Rad ographs may reveal lesions of osteitis fib osa cysti a

Hype p tu tarism (p 1225)
Prognathism in acromegaly with eno mou increase n size of mand ble overdev loped an l forwa d jutting ch n w de s paration of lower teeth pa t cularly incisors lower lip thick ned an l everted tongue furrow d and greatly enlarged often protruding from mouth

Ad l Cort l Def ncy (Add son s D s se) (p 1 71)
P gm ntation of mouth usually se n on l ps anterior gums and buccal mucosa precedes skin ch nges as sharply deli eated dark brown to blue bla k pa l ss l s ons (See Fig 346)

TABLE 115—ORAL MANIFESTATIONS OF INFECTION (Continued)

Secondary Syphilis (p 331)

Vivid erythema of soft palate and fauces associated with pain on swallowing enlargement and tenderness of cervical lymph nodes later mucous patches which appear as painless indurated oval ulcers approximately 2 cm in length chiefly found on floor of mouth inner surface of lip and dorsum or ventrum of tongue edges slightly elevated and red with central depression covered by grayish white membrane distribution usually symmetrical with later confluence split papule appears bilaterally at the commissures of the lips extending over the skin as semicircular lesions with sharply defined indurated borders

Diagnosis by darkfield and serology

Tertiary Syphilis (p 331)

Gummas may appear on lips hard palate soft palate or tongue soft painless swellings with indurated bases later ulceration with production of a dark red cauliflower base and tissue destruction specific response to iodine interstitial glossitis less frequent than gumma begins as diffuse infiltration of organ followed by erosion and loss of papillae tongue may become furrowed and lobulated (See Fig 34°)

Diagnosis may be obscured by negative serology



Fig 315—Foot and mouth disease

Prenatal Syphilis (p 2787)

Rhagades consist of thin linear scars radiating from the commissures of the lips Hutchinson s teeth occur with secondary dentition as characteristic hypoplasia of the biting edges of the upper anterior or lower anterior teeth central incisors narrow tapering and notched at the biting edge first molars exhibit generalized hypoplasia on grinding surfaces cusps small pointed and closely clustered together

Diagnosis by serologic tests

Tuberculosis (p 25°)

Ulcers may appear on lips tongue palate or gums original appearance as small red nodules with later ulceration ulcers appear sharly defined with tendency to coalesce producing large irregularly shaped lesions with blue margins and a depressed center covered by gray exudate pain severe and accompanied by hypersalivation and lymphadenitis (See Fig 313)

Diagnosis by biopsy

Clough Bull Johns Hopk ns Hospital

preparation is indicated in the management of disturbances of gums and tongue which fail to respond to local forms of treatment

TABLE 117.—ORAL MANIFESTATIONS OF NUTRITIONAL DEFICIENCIES

Vitamin A Deficiency (p 619)

In experimental animals insufficiency of A interferes with proper calcification of dentine clinical deficiency may produce keratoses or leukoplakia

Therapeutic test with vitamin A

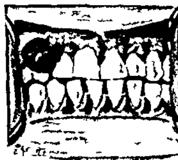


Fig 350—Gingivitis gravidarum with pregnancy tumor

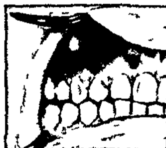


Fig 351—Thrombocytopenic purpura (hemorrhagica)

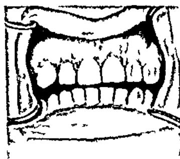


Fig 352—Halo saturninus (lead line)

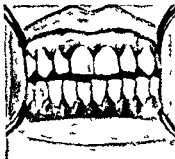


Fig 353—Bismuth deposit in gingivae

Thiamin Deficiency (p 622)

Burning sensation of tongue mild pain in face

Specific relief from administration of vitamin B complex

Riboflavin Deficiency (p 622)

Cheilosis gingivitis and lesions of tongue dryness and narrowing of exposed vermilion tissue of lip with lateral areas of desquamation similar patches adjacent to alae thin linear rhagades radiate outward from commissures of lip persistent red desquamated area (perleche) may be superimposed on rhagade salivary secretion diminished tongue enlarged with reddened tip and borders inflamed papillae may appear scattered over tip and dorsum mild gingivitis leading to sloughing with secondary fusospirillosis (See Fig 348)

Therapeutic test with riboflavin

Thoma Oral Diagnosis

TABLE 116—ORAL MANIFESTATIONS OF ENDOCRINE DISTURBANCES (*Continued*)

Diabetes Mellitus (p 1246)

Acetone odor to breath dryness of mouth with cyanosis of mucous membranes enlargement and fissuring of tongue with areas of papillary denudation gums inflamed beefy and easily provoked to bleeding large deposits of soft white tartar encru t lower an *terior and upper molar teeth* early recession of gums with loosening of teeth and erosion of their necks Many of latter manifestations probably representative of accompanying avitaminoses



Fig 346—Pigmentation in Addison s disease



Fig 347—Hunterian glossitis in macrocytic hyperchromic anemia



Fig 348—Magenta tongue and cheilosis of vitamin B deficiency



Fig 349—Teeth in rickets

Gonadal Dysfunction (p 2593)

Long continued administration of estrogen may lead to hyperplasia of gingival t ssues protracted admini tration of progesterone sometimes followed by ulcerative gingivitis in pregnancy gum margins often red with easy bleeding saliva ropy and profuse islands of *proliferative gingivitis may develop and progress to formation of* epulides with persistence as fibromas or giant cell tumors (p 1715) tumors often deep red to purple and may vary in size from pea to almond dental caries no more frequent in pregnancy than in nonpregnant but destruction of dentine once initiated progresses more rapidly (See Fig 350)

ORAL MANIFESTATIONS OF NUTRITIONAL DEFICIENCIES

Lack of teeth and reduced alimentation may result in subvitaminoses (p 616) common oral manifestations are *glossitis and gingivitis* the latter occurs in areas where oral hygiene is defective whereas adjacent edentulous zones are unaffected A therapeutic test with a polyvalent vitamin

TABLE 118 — ORAL MANIFESTATIONS OF THE BLOOD DYSCRASIAS (Continued)

Polycythemia Vera (p 1093)
Purplish red color to lips oral mucosa and tongue isolated ecchymoses most frequent on hard palate gums tender and bleed easily chronic gingivitis leads to loosening of teeth
Diagnosis from hemogram local *treatment* palliative

Hemophilia (p 1118)
Bleeding from gums persistent and protracted
Diagnosis from history and prolonged clotting time

Thrombocytopenic Purpura (p 1114)
Petechiae on soft palate and fauces widespread ecchymoses hemorrhagic spots on gums in vestibule or on inner surfaces of lips papillary oozing from gums small spherical hemorrhagic blebs at gum margins and on buccal mucosa (See Fig 351)
Diagnosis from platelet count local *treatment* palliative

Leukemia (p 1100)
Spontaneous bleeding from gums hypertrophy of interdental papillae gingival mucosa edematous and flabby looking in later phases exudate with ulceration of gum margin hypersalivation and fetid odor to breath painful submandibular lymphadenitis with secondary fusospirillosis
Diagnosis from hemogram local *treatment* palliative

Infectious Mononucleosis (p 466)
Gums red spongy and bleed easily marked enlargement of submandibular lymph nodes
Diagnosis from hemogram and heterophile reaction

Agranulocytosis (p 1096)
Severe stomatitis with secondary fusospirillosis rapidly ulcerating lesions with sharply demarcated borders ulcers covered with putrid yellow gray tenacious slough bone denuded with later necrosis and sequestration
Diagnosis from hemogram local *treatment* palliative

Hereditary or Congenital Telangiectasia (p 1119)
Oral lesion occurs with great frequency and may be plain otherwise undiagnosed bleedings from respiratory and intestinal tracts
Local *treatment* palliative

ORAL MANIFESTATIONS IN POISONING BY METALS AND NONMETALS

Several drugs and poisons produce typical reactions in the mouth Deposits of tartar pre existing gingivitis and inflamed gum flaps covering partially erupted third molars generally determine the site and the extent of the lesion or deposition Disturbances rarely occur in healthy mouths or the edentulous

TABLE 119 — ORAL MANIFESTATIONS OF POISONING BY METALS AND NONMETALS

Plumbism (p 769)
Deep blue pigmentations along gingival margins of upper and lower teeth due to deposition of lead sulfide in a succession of discrete spots pigmentation occurs only where there is gingivitis due to faulty dental hygiene (See Fig 352)
Diagnosis from history blood spread and urine tests

Bismuth Poisoning (p 129)
Bismuth line resembles lead line except for color which is gray or black associated with mild gingivitis hypersalivation and submandibular lymphadenitis (See Fig 353)
Diagnosis from history and urine tests

TABLE 117—ORAL MANIFESTATIONS OF NUTRITIONAL DEFICIENCIES (*Continued*)

Niacin Deficiency (p 625)

Gums painful with easy bleeding mouth dry and sore burning sensation in cheeks and tongue tongue reveals small oval patches covered by superficial white membrane so that organ appears spotted lesions erode and spread in all directions becoming confluent so that organ appears edematous raw and of a characteristic magenta color hypersalivation accompanies ulcerating lesions frequent secondary fusospirillosis

Therapeutic test with niacin

Sprue (p 1938)

In acute stage soreness of mouth with glistening red spots on tongue surrounded by yellow gray area of slough continued papillary destruction results in denudation and soreness of tongue in chronic or relapsing phase tongue enlarged highly glazed and deeply fissured painful yellow ulcers on gums and cheeks

Diagnosis by therapeutic test with liver extract

Vitamin C Deficiency (Scurvy) (p 2857)

Gingival ecchymoses hypersalivation bleeding of interdental papillae later ulceration of gums with destruction of soft tissue loosening of teeth and fetid odor to breath

Diagnosis by therapeutic test with cevitamic acid

Vitamin D Deficiency (Rickets) (p 2850)

Osseous symptoms lead to characteristic facies elongated cranium narrow upper jaw with protruding anterior teeth retracted and underdeveloped chin and widely separated lips palatal vault high arch of upper teeth V shaped with prominent central incisors upper and lower anterior teeth widely separated when jaws are closed marked delay in primary dentition permanent teeth overcrowded and may fail to erupt incisors markedly hypoplastic with pitting of enamel at or near the biting edges (See Fig 319)

Diagnosis from clinical syndrome

ORAL MANIFESTATIONS OF BLOOD DYSCRASIAS

The blood dyscrasias (p 1085) consistently display diagnostic clues in the mouth Oral lesions generally precede other clinical symptoms and may lead to the early diagnosis of the fundamental disturbance Secondary fusospirillosis is so frequently superimposed on the oral manifestations of blood disease that a hemogram is indicated in any instance in which the Vincent organisms are demonstrable (p 50)

Disturbances of the hematopoietic system are often associated with intractable spontaneous or post extraction bleeding These are treated by the use of Monsel s solution or powdered tannic acid applied with sustained pressure (p 1665) Fibrin foam has been successfully employed in controlling oral bleeding in hemophilia

TABLE 118—ORAL MANIFESTATIONS OF THE BLOOD DYSCRASIAS

Macrocytic Hyperchromic Anemia (p 1071)

Palatal mucous membranes pale stinging or burning sensation of tip of tongue redness slight swelling and tenderness of tongue with later epithelial desquamation leading to complete disappearance of papillae and decrease in size of tongue (Hunterian glossitis) final appearance of a smooth and glistening surface with a dry mouth (See Fig 317)

Diagnosis from hemogram

Aplastic Anemia (p 1090)

Recurrent and uncontrollable bleeding from gums ecchymoses of hard palate diagnosis from hemogram

Local *treatment* palliative

CHAPTER 83

CLINICAL DISTURBANCES OF THE OROPHARYNX ORAL INTERRELATIONSHIPS SYSTEMIC EFFECTS OF ORAL DISEASE (FOCAL INFECTION)

The close proximity of the oropharynx to the nasopharynx and the upper respiratory and digestive structures leads to a reciprocal spread of inflammatory processes Oral lesions may involve neighboring tissues by continuity and contiguity and vice versa additionally oral infection may cause focal infection in distant structures

ORAL INTERRELATIONSHIPS

The Nose —*Acute dento alveolar abscesses* arising from the upper central incisor teeth occasionally discharge spontaneously into the inferior meatus of the nose The fistula so produced generally persists until the offending tooth has been removed

The Maxillary Antrum —Periapical infection of the posterior teeth of the upper jaw may be the primary cause or an aggravating factor of an *antral empyema* (p 2126) With persistent unilateral infection of a maxillary sinus it is logical to advise the removal of infected contiguous teeth Relief is often effected without further treatment

Acute maxillary sinusitis (p 2125) may follow upon tooth extraction the floor of the antrum is sometimes perforated in the operation leading to infection of the sinus by oral micro organisms

The Throat —*Enlarged adenoids* and *tonsils* and *irregularities of the nasal septum* promote mouth breathing which through constriction of the nasal fossae often produces a *high palate* and *irregularities in the positions of teeth* Before the beginning of corrective procedures by the orthodontist the effects of removal of underlying defects should be observed

The Floor of the Mouth —*Dental abscesses* whether non operative or due to post extraction infection in the lower jaw may extend along the fascial planes to produce swellings of the soft palate or faucial isthmus Without regard to the etiologic factor these potentially serious lesions require anti infective therapy (p 106) with sulfonamides and/or penicillin and incision for drainage as soon as there is fluctuation or localization Later the patient is referred to the oral surgeon for eradication of the causative disturbance

The Ear.—*Tinnitus* (p 2141) and *pains* in the parietal temporal and masseteric regions of *elderly patients* often result from abnormal closure of the bite Malocclusion follows attrition or loss of teeth and influences the facies by reducing the original measurement from the base of the nose to the chin the lip line is thinned and lengthened deep linear depressions radiate from the commissures *Pain* is engendered by pressure on nerve endings due to a disturbed anatomical relationship of the mandibular condyle in the glenoid cavity

TABLE 119—ORAL MANIFESTATIONS OF POISONING BY METALS AND NONMETALS (Continued)

Mercury Poisoning (p 765)

Metallic taste hypersalivation and putrid odor to breath severe gingivitis with slou h ing and ulceration heavy coating of tongue with edema and indentation of borders by pressure against teeth later tenderness of teeth loosening and submaxillary lymph adenitis

Diagnosis from history and urine tests

Iodism (p 612)

Hypersalivation with pain and swelling of salivary glands and edema of buccal mucosa

Diagnosis from history

Radiation Sickness (p 3798)

Exposure to roentgen ray or radium may produce aseptic osteomyelitis of jawbones particularly the mandible later necrosis from secondary infection

Diagnosis from history local *treatment* palliative and surgical

Phosphorus Poisoning (p 729)

Odontalgia followed by localized swelling and tenderness in vicinity of carious mandibu lar teeth later loosening and loss of teeth with extensive suppurative osteitis and necrosis sinus formation malodorous breath and hypersalivation (phossy jaw)

Diagnosis from history local *treatment* palliative

Fluorine Poisoning (p 755)

Mottled enamel due to high concentration of fluoride in drinking water large irregu lar opaque spots later becoming pitted and brown appear on enamel of teeth high degree of immunity to dental caries

Diagnosis from water analysis local *treatment* ineffectual for removal of stains

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The *diagnosis* may be verified by the relief of symptoms when the intermaxillary space is increased A tongue depressor is introduced between the posterior teeth while the patient bites down firmly A suitable splint or denture affords permanent relief

The Bronchi and Lungs —Septic material from the oropharynx aspirated into the bronchi during periods of unconsciousness may cause *postoperative pneumonitis* (p 2189) or *abscess of the lung* (p 2215) Dental prophylaxis is an important preventive measure before operation and in the care of patients whose gagging or cough reflexes are dulled during comatose episodes or through the extended use of hypnotics

DIFFERENTIAL DIAGNOSIS OF

Toothache (Odontalgia)

Dental pain may be most confusing It is often difficult to determine whether the disturbance is of local origin or a reflection of an abnormality involving eye ear or throat At times differentiation is exceedingly perplexing and may require consultation with dental surgeon, otologist rhinologist and ophthalmologist

	DIAGNOSTIC FEATURES
Oral	From stomatitis gingivitis pyorrhea alveolaris glossitis or dental caries In pulpitis note greater sensitivity to cold (p 1704) In pericementitis note greater sensitivity to heat (p 1704) Observe x ray changes in fracture dento alveolar abscess and osteomyelitis of mandible maxilla or tooth sockets
Rhinogenic	Particularly with infections cysts and neoplasms involving maxillary antrum Get x rays and examine returns from lavage (p 2128)
Otogenic	Referred pain particularly in otitis media purulenta acuta with bulging ear drum
Ophthalmic	In iritis with circumcorneal injection
Psychogenic	In hysteria
Neurogenic	From sphenopalatine neuralgia of Sluder with relief from cocainization of reg on of ganglion (p 1482) From trigeminal neuralgia with relief from alcohol injection (p 1482)
Neoplastic	Particularly with malignancies involving oropharyngeal structures Identify by biopsy

Putrid abscess of the lung (p 2215) may occur in healthy patients through direct aspiration of dislodged fragments of septic tartar The inhaled fragment lodges in a small caliber bronchiole and an anaerobic infection is produced Most patients with *idiopathic abscesses of the lung* are found to have heavy incrustations of tartar on the lingual surfaces of the lower anterior teeth

Digestive Disorders —Absence of teeth results in surprising little effect on the digestion of the common foodstuffs Even the completely edentulous ordinarily maintain nutrition in a satisfactory manner

Edentate Gastritis —Very occasionally the edentate develop a *chronic*

gastritis (p 1810) Under these circumstances dentures are prescribed for the relief of the resultant metabolic or gastric disorders

Catarrhal Stomatitis—Dietary indiscretion and excessive drinking or smoking may produce a transient catarrhal stomatitis characterized by dryness and soreness of the mouth furring of the tongue and fetid odor to the breath This condition is graphically described in the alcoholic hang over as resembling the "bottom of a bird cage

The sense of taste is considerably diminished the tissues of the mouth are red and tender and aphthae may appear recurrently in the mouth

Glossitis with Achlorhydria—In achlorhydria the tongue may become denuded of its papillae it presents a pale smooth glistening appearance



Fig 3 4—Unerupted third molar The postero-anterior view (nose-chin position) shows the third molar high in the maxillary sinus there is cloudiness of the entire left sinus *

the patient complains of a burning or painful sensation which may be relieved by the enteral administration of dilute hydrochloric acid (p 1753)

FOCAL INFECTION

Pyorrhea alveolaris (p 1700) and *chronic periapical abscess* may produce distant inflammatory lesions despite slight local discomfort In many instances the focus of infection is identified solely by dental roentgenograms *Pyorrhea alveolaris* appears in the film as a loss of the alveolar process adjacent to the tooth *chronic periapical abscess* is demonstrated

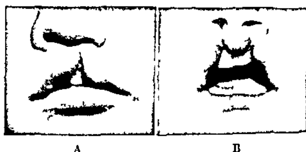
* McCall and Wald Clinical Dental Roentgenology

the sidewise pressure of the erupting lateral incisors Should it persist beyond the age of ten years the redundant portion is removed

FORDYCE S CONDITION

The entity described by Fordyce is an anomalous distribution of *sebaceous glands* immediately beneath the labial or buccal mucosa It is found among a large percentage of adults its discovery perplexes and disturbs the patient although it is symptomless

The lesion is located on the lips just inside the commissures in the form of slightly elevated *brownish patches* When the involved tissue is stretched the patches appear to consist of a large number of tiny tan



A B

Fig 356 — Harelip *A* Unilateral *B* Bilateral (Kazanjian)



Fig 357 — Fordyce s disease affecting upper lip

papules Similar patches may occur on the buccal mucosa opposite the molar teeth on the glans penis and the labia minora The condition may persist throughout life but requires no treatment (See Fig 357)

CLEFT TONGUE (BIFID TONGUE)

Congenital clefts of the tongue are much less common than those of the lips or palate The defect occurs in the midline and seldom extends more than a centimeter beyond the tip It rarely interferes with function but its unesthetic appearance sometimes makes surgical correction desirable

MACROGLOSSIA

Congenital macroglossia is a stigma of *cretinism* (p 1191) or more rarely of *prenatal syphilis* (p 2787) Improvement is possible by plastic

DIFFERENTIAL DIAGNOSIS OF

Disturbances of the Lip

Lesions of the lip may represent local or systemic disturbances The latter may be of grea variety and include infectious metabolic and endocrinologic disturbances

	DIAGNOSTIC FEATURES
Congenital Anomalies	Harelip macrocheilia elongated labial frenum and Fordyce condition
Physical and Chemical Injuries	Trauma burns and frostbite Dehydration with sordes
Dermatoses	Dermatitis factitia from picking in psychogenic disturbance Lupus erythematosus with cutaneous exanthem
Local Inflammations	Perleche with therapeutic response to vitamin B complex Furuncle or carbuncle with widespread edema and constitutional manifestations particularly if located on upper lip
Systemic Infections	Herpes simplex or zoster with characteristic vesicle (p 435) Primary or secondary syphilis with positive darkfield microscopy and/or serology Erysipelas with intense swelling and constitutional manifestations (p 167) Foot and mouth disease with associated lesions on extremities (p 437) Tuberculosis with acid fast organisms demonstrable in smear or biopsy
Neoplasms	Angiomas and other benign growths Epitheliomas with distinctive biopsy findings (p 1717)
Allergy	Contact dermatitis particularly from lip stick (p 1669) Angioneurotic edema from physical allergy (p 1670) Digestants or drugs
Metabolic Disturbances	Avitaminoses with rhagades and therapeutic response to vitamin B complex
Endocrinopathies	Thickened lips in cretinism with lowered B M R and therapeutic response to thyroid extract Protruding lips in acromegaly with characteristic skeletal change and prognathu
Neurogenic	Asymmetry and drooling with facial paralysis Tremor in paralysis agitans general paresis and epidemic encephalitis Get blood and spinal fluid serology and colloidal gold reaction

surgery in selected cases Congenital *cavernous angiomas* may simulate macroglossia

TONGUE TIE

Incomplete development of the lingual frenum results in limitation of movement of the tongue and interference with *speech* (p 1310) Should the defect persist beyond infancy simple section of the frenum is indicated

FISSURED TONGUE (GROOVED TONGUE SCROTAL TONGUE)

Fissured tongue is a common congenital condition unassociated with any definite etiology The dorsum exhibits a pattern of smooth grooves of varying length and depth radiating in symmetrical undulating furrows from a sharply depressed median raphe The furrows surround islands of normal papillated tissue (Fig 358) A variant of the fissured tongue consists of an intertwining arrangement of grooves coupled with papillary atrophy of the islands so that the dorsum strongly resembles the surface of the scrotum (*scrotal tongue*)

The fissured tongue becomes inflamed when condiments tobacco and food fragments are retained in its crypts Restriction of dietary irritants and mouth washes of sodium bicarbonate are indicated to relieve soreness



Fig 358—Scrotal tongue



Fig 359—Geographic tongue

GEOGRAPHIC TONGUE

Geographic tongue is a wandering *desquamation* of the superficial layers of the dorsum It usually begins in childhood and persists into adult life

The initial lesion is a slightly discolored spot which presently dissolves into a small oval erosion bright red in the center with a raised periphery of yellowed hypertrophic papillae The erosion spreads in ameboid fashion denuding the tongue as it advances and healing at other points so that it appears to be migrating New patches appear and coalesce as maturer patches begin to resolve producing a *maplike appearance* The lesions finally disappear only to recur in a fresh cycle (See Fig 359)

The dorsum of the tongue is almost always the sole seat of the disease the condition being more prominent towards the tip and sides In general there are no subjective symptoms other than anxiety

Treatment is not particularly successful although cures with radium and roentgen rays have been reported Simple mouth washes and improvement of the general health are all that are needed in the average case

CLEFT PALATE

Congenital cleft palate is a deformity due to lack of union of the lateral halves of maxilla or soft palate It may involve the *soft palate* alone

DIFFERENTIAL DIAGNOSIS OF

Disturbances of the Tongue

Lesions of the tongue must be regarded with considerable gravity since they often rer resent profour d local or systemic disturbances

	DIAGNOSTIC FEATURES
Congenital Malformations	Macroglo ia and tongue tie Cl ft palate and fissured or geographic tongue
Physical and Chemical Injuries	Burns Bites particularly in epilepsy Black hairy tongue from mouth washes containing perborate
Local Inflammations	Aphthous glossitis Absce s of tongue Moeller s glossitis with therapeutic response to liver extract de spite normal hemogram Glossitis rhomboide a mediana with bluish induration in median line Leukoplakia Ludwig s angina involving floor of mouth
Systemic Infections	Scarlet fever with strawberry tongue (p 171) Primary and secondary syphilis with positive dark field microscopy and/or serology Tertiary syphilis with therapeutic response to iodide Actinomycosis with ray fungus in exudate or scrapings Tuberculous ulcer with acid fast organisms in smears or bipo y (p 1672)
Metabolic Disturbances and Endocrinopathies	Avitaminosis with magenta color glossitis and glossodynia responding to thiamine riboflavin or niacin. Dehydration with dryness and sordes Autointoxication with coating of tongue Cretinism with protru ion of tongue low BMR and therapeutic response to thyroid extract Acromegaly with enlargement of tongue and skeletal changes
Allergy	Angioneurotic edema
Dermatoses	Lichen planus pemphigus and dermatiti herpetiformis with associated cutaneou eruptions
Neoplasms	Ranula angioma papilloma epithelioma or carcinoma Corroborate findings by biopsy (p 1718)
Hematologic	Hunterian atrophic glossitis with macrocytic hyperchromic anemia and therapeutic response to liver extract. Hemorrhagic le ions in thrombocytopenic purpura and leukemia with characteri tic hemograms
Neurogenic	Tremor in paralysis agitans general paresis multiple sclerosis and alcoholism. Supplement neurologic examination with serologic and spinal fluid examination (p 3734) Hemiparesis with organic lesions of hypoglossus
Psychogenic	Glossalgia and glossodynia In hysteria

or continue forwards to include the *alveolar ridge* exposing the nasal floor It is often associated with *cleft lip* and exhibits a familial tendency

Cleft palate poses an early problem in infant feeding The opening may be covered with a small dental plate or a *cleft palate nipple* may be employed until the child is ready for corrective surgery Speech defects and impaired resonance of the voice persist if plastic repair is postponed too long after the child has learned to speak When cleft palate is inoperable



Fig 860 —Torus palatinus



Fig 861 —Bird face appearance caused by underdevelopment of jaw due to ankylosis

or surgery is unsuccessful an artificial *dental obturator* may be constructed to cover the defect and improve phonation

TORUS PALATINUS

An abnormal projecting elevation of bone of variable shape and size may be found at the center of the *hard palate* The torus palatinus is barely palpable in childhood begins to be prominent in adolescence and

* Thoma in Pullen Medical Diagnosis

attains its greatest size after the fourth decade It is hard and covered with normal rugate mucous membrane Although the torus presents most of the characteristics of a slowly growing *osteoma* surgical removal is indicated only when there is interference with the retention of an artificial denture Tori must be differentiated from neoplasms of the palate particularly mixed tumors (p 1717) (See Fig 360)

ANKYLOSIS OF THE TEMPOROMANDIBULAR JOINT

At birth or in the newborn period one or both temporomandibular joints may be ankylosed usually as a sequence to *birth trauma* involving the mandibular condyle An associated overgrowth of cicatricial tissue in the glenoid fossa further limits movement subsequently *calcification* of scar tissue virtually eliminates mandibular motion Because of this fixation neither mandibular nor submaxillary muscles develop properly and the child acquires a birdlike facies (Fig 361) the jaw is retracted and the face flattens on the side opposite to the ankylosed joint Treatment is surgical

PHYSICAL AND CHEMICAL INJURIES

In spite of the many opportunities for physical and chemical traumas to the oral cavity remarkably few lesions of significance are observed in clinical practice

WOUNDS

Oral wounds require thorough cleansing with 3 per cent hydrogen peroxide the application of powdered sulfanilamide and coaptation with *braided black silk sutures Accurate repair is required in lacerations of the* lips or tongue in order to preserve function and appearance No dressing is needed secondary infection is rare antitetanus injections are given for the same indications as for wounds elsewhere (p 297)

Ulcer of the Lingual Frenum—The base of the frenum of the tongue may become deeply ulcerated as a result of irritation from a lower denture or from explosive coughing particularly in *whooping cough* (p 278) Most ulcers yield to repeated applications of 10 per cent silver nitrate Persistent ulcers may be cancerous and a biopsy is advisable upon slight suspicion

BURNS

Scalds or *superficial chemical burns* usually involve the *hard palate* or *tongue* The epithelial surface presents a shriveled appearance and is covered with a white or brown desquamating membrane Although the lesions generally heal spontaneously mouth washes of *milk of magnesia* are used to soothe the parts

Induration and deep ulceration may occur in severe burns Initial disinfection is secured by a liberal spread of 1 per cent solution of *Gentian Violet* Later the mucosa is irrigated with lukewarm saline solution and painted with Glycerite of Tannin A thick paste of Ethyl Aminobenzoate is used for the relief of severe pain

Extensive third degree burns such as those produced by burning oil may be treated by sprays of Pickrell s solution (3 per cent sulfadiazine in

8 per cent Triethanolamine) Systemic therapy follows the principles elsewhere discussed (p 3981)

GALVANISM

Through the agency of the saliva which serves as an electrolyte electrogalvanic irritation may be produced by fillings of widely dissimilar metals As a rule the symptoms are mild and consist of an acrid *metallic taste* (taste of tinfoil) or a slight *burning sensation* at the tip of the tongue At times an acute twinge of *dental* (p 1618) or *otitic pain* (p 2143) is experienced at the moment that the teeth are brought together and the metal fillings come in contact For the most part this condition adjusts itself through a protective calcification of the horns of the dental pulp When it persists the faulty fillings are replaced with bland cement

Electrolytic action sometimes produces deeply inflamed patches of *blanched tissue, and erosive zones on palate tongue or gums* These occur at points of contact of large dentures constructed of base metals Relief follows removal of the cause

DENTURE CHEILOSIS

Defective closure of the bite due to attrition of the natural denture or maladjusted artificial dentures causes the lips to become long and narrow The resulting invagination of the orbicularis muscle at the labial corners produces deep diagonal wrinkles Drooling of *saliva* at the commissures causes maceration and lesions which bear striking similarity to *perleche* (p 1693) and *ariboflavinosis* (p 1675)

The treatment is mechanical by correction of the bite

TRAUMATIC STOMATITIS

A traumatic stomatitis may be produced by irritation from irregular teeth deposits of tartar ill fitting dentures strong chemicals and excessively hot food The condition requires removal of the cause and local palliation

TRAUMATIC GINGIVITIS

Traumatic gingivitis may be due to the overzealous use of detergent tooth powders or toothpastes (p 1661) or to an abnormal bite pressure involving pairs of antagonizing teeth The latter is a traumatic occlusion which exerts continual stress on the peridontal tissues during mastication As a result circulatory changes occur in the gum margins producing hypertrophy or atrophy Additional local irritation may result from overhanging fillings crowns that impinge on the mucosal surfaces poorly fitting dentures food debris and trauma from toothbrush bristles or toothpicks Treatment is palliative and corrective

BEDNAR STOMATITIS

Bednar stomatitis is a bilateral spreading ulceration of the palate it is caused by maladapted nursing devices

TRAUMATIC GLOSSITIS

Irritation from the rubbing of jagged teeth or ill fitting dentures and biting of the tongue may produce generalized inflammation, traumatic

ulcer lingual abscess or a neoplasm Traumatic glossitides are character ized by intense pain which interferes with eating and speaking

Treatment consists in removal of the cause and the frequent use of warm alkaline mouth washes *traumatic ulcer* is treated by several daily applications of 10 per cent silver nitrate solution *abscess of the tongue* may require incision and drainage the symptoms and treatment of *neo plasms* are considered elsewhere (p 1714)

LEUKOPLAKIA

Leukoplakia which affects patients past the fourth decade appears to be associated with subvitaminosis liberal indulgence in tobacco strong alcoholic drinks and jagged teeth It is said to occur with *syphilis* but this must be rare according to our experience

Clinical Manifestations—Leukoplakia is a chronic painless *keratiniza tion* of the oral mucosa of the dorsum of the tongue the cheek the lip or the hard palate It develops gradually in well defined dry white *plaques* which may be diffuse smooth and superficial or more circum scribed and elevated In any instance the lesions are distinctly palpable giving an impression of hardness and superficial roughness but rarely of induration (Fig 362)

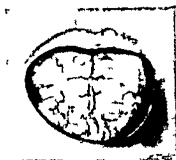


Fig 362—Leukoplakia

Diagnosis—Leukoplakia is to be differentiated from *lichen planus* (p 1667) and the oral manifestations of *avitaminosis* (p 1675) Each of the latter is recognized through associated lesions elsewhere

Course—Leukoplakia runs a chronic course and as a result of con tinued traumatization the patches develop deep erosions that may un dergo malignant *degeneration* although this occurs more rarely than is commonly reported

Treatment—Tobacco alcohol and spices are interdicted in patients ex hibiting eroded lesions The teeth are freed from irritating projections and a regimen of strict oral hygiene is instituted Mild alkaline mouth washes are of value in reducing the soreness of inflamed plaques Massive doses of vitamin A and of riboflavin are often beneficial

The value of radium or roentgen ray irradiation in simple leukoplakia is questionable as few lesions are malignant Small patches that are in clined to become recurrently inflamed should be regarded as precancerous (p 571) and are cautiously removed by surgical excision

Thoma Oral Diagnosis

8 per cent Triethanolamine) Systemic therapy follows the principles elsewhere discussed (p 3981)

GALVANISM

Through the agency of the saliva which serves as an electrolyte electrogalvanic irritation may be produced by fillings of widely dissimilar metals As a rule the symptoms are mild and consist of an acid *metallic taste* (taste of tinfoil) or a slight *burning sensation* at the tip of the tongue At times an acute twinge of *dental* (p 1618) or *otitic pain* (p 2143) is experienced at the moment that the teeth are brought together and the metal fillings come in contact For the most part this condition adjusts itself through a protective calcification of the horns of the dental pulp When it persists the faulty fillings are replaced with bland cement

Electrolytic action sometimes produces deeply inflamed patches of blanched tissue and erosive zones on palate tongue or gums These occur at points of contact of large dentures constructed of base metals Relief follows removal of the cause

DENTURE CHEILOSIS

Defective closure of the bite due to attrition of the natural denture or maladjusted artificial dentures causes the lips to become long and narrow The resulting invagination of the orbicularis muscle at the labial corners produces deep diagonal wrinkles Drooling of *saliva* at the commissures causes maceration and lesions which bear striking similarity to *perleche* (p 1693) and *ariboflavinosis* (p 1675)

The treatment is mechanical by correction of the bite

TRAUMATIC STOMATITIS

A traumatic stomatitis may be produced by irritation from irregular teeth deposits of tartar ill fitting dentures strong chemicals and excessively hot food The condition requires removal of the cause and local palliation

TRAUMATIC GINGIVITIS

Traumatic gingivitis may be due to the overzealous use of detergent tooth powders or toothpastes (p 1661) or to an abnormal bite pressure involving pairs of antagonizing teeth The latter is a traumatic occlusion which exerts continual stress on the peridontal tissues during mastication As a result circulatory changes occur in the gum margins producing hypertrophy or atrophy Additional local irritation may result from overhanging fillings crowns that impinge on the mucosal surfaces poorly fitting dentures food debris and trauma from toothbrush bristles or toothpicks Treatment is palliative and corrective

BEDNAR STOMATITIS

Bednar stomatitis is a bilateral spreading ulceration of the palate it is caused by maladapted nursing devices

TRAUMATIC GLOSSITIS

Irritation from the rubbing of jagged teeth or ill fitting dentures and biting of the tongue may produce generalized inflammation traumatic

CHAPTER 85

CLINICAL DISTURBANCES OF THE OROPHARYNX INFLAMMATIONS AND INFECTIONS

The oropharynx is often the site of localized inflammatory and infectious processes which may resemble the manifestations of systemic disturbances previously described (p 1607)

CHEILITIS

The mucocutaneous junction of the lip may be involved in acute or chronic inflammatory disturbances Mild lesions consist of slight redness and swelling in the more severe involvement there may be edema crusting and scaling with chronic forms fissures are noted at the angle of the mouth and precancerous keratoses (p 1717) may develop

Treatment —The local treatment of cheilitis is symptomatic Acute processes are best allayed with cold wet applications chronic forms are treated with camphor ice or 1 per cent ointment of ammoniated mercury Persistence of the lesion despite adequate local therapy engenders the suspicion that there is some additional etiologic factor such as *syphilis* (p 331) *avitaminosis* (p 616) or *malignancy* (p 572) Under these circumstances diagnostic investigations are broadened to include darkfield examinations blood serology and histological studies therapy is then directed at the more serious disturbance

PERLECHE

Perleche is a special type of cheilitis which is noted in undernourished infants and less frequently in older children and adults It is a mild but persistent infection that is due to invasion by *streptococci* or *Monilia albicans* (p 502) In its early stage it appears as a bilateral white fan shaped discoloration at the angles of the lips The associated sensation of dryness causes the patient to moisten the area with the tongue As a result the skin becomes macerated fissured and later encrusted with dry scabs (Fig 365)

FRACTURES

Fractures of the mandible occur with far greater frequency than fractures of the maxilla They generally result from injuries in automobile collisions or from blows of the fist Most fractures are *compound* and there is often intra oral bleeding pain on movement of the mandible and hypersalivation Although there may be little or no external deformity a marked discrepancy in the interlocking relationship of the closed teeth may be observed due to the pull of the depressor muscles on the loose segment of bone *Roentgenograms* are essential in suspected fracture of the jaws as breaks in the ascending ramus and condyle are easily over looked

Emergency Treatment by the Practitioner—When specialist treatment is not immediately available emergency measures are required for the control of shock and hemorrhage and the immobilization of the fragments The last is conveniently accomplished by the use of the four tailed bandage The center or wide portion of the bandage is placed beneath the forepart of the mandible and the anterior wings are fastened over the center of the cranium The posterior tails are carried behind the ears and knotted over the occipital protuberance As the bandage is tightened and tied the chin should be forced upwards and forward so that the lower teeth are brought firmly into interlocking contact with the upper teeth forming a satisfactory splint

In compound fractures prophylactic use of the sulfonamides (p 88) or penicillin (p 106) is highly desirable

Treatment by Specialist—The oral surgeon should be consulted for the construction of special devices and wiring to secure coaptation and im *mobilization*

DISLOCATION OF TEMPOROMANDIBULAR JOINT

The mandible may become suddenly dislocated as a result of a sharp blow on the chin or a violent yawn The patient feels a snapping sensation in the temporomandibular joint and is unable completely to close the jaws Generally the luxation is forwards resulting from the escape of the mandibular condyle from its seat in the glenoid fossa to the interarticular eminence

To reduce the dislocation it is necessary to force the condyle downwards thereby eliminating the obstruction offered by the eminence and then to apply pressure backwards This is accomplished by pressing forcibly downwards on the lower posterior teeth simultaneously pushing the mandible posteriorly The operator s fingers should be protected by a pad of gauze General anesthesia facilitates the maneuver by relaxing the muscles Aftercare involves the use of a soft diet and warning to avoid wide opening of the jaw for several weeks

10 grs) three times daily This prescription has elements of toxicity and small promise of significant usefulness For local application the under noted is often employed

℞	Potassium Chlorate	10 0
	Glycerin	50 0
	Water q s a d	180 0
	Sg Local application	

Ulcerated lesions may be touched with 1 per cent *Acriviolet Compound Tincture of Benzoin* or 10 per cent *Silver Nitrate* If the lesion is per sistent local therapy is supplemented by parenteral vitamins and the anti infective agents using sulfonamide locally and penicillin locally or by in tramuscular injection

INFECTIOUS STOMATITIS

Infectious stomatitis sometimes follows influenzal types of pharyngitis particularly among small children A mild oral discomfort is noted after remission of the pharyngeal oreness At this time a scarlet *erythema* is observed involving the palate Spread is rapid to the cheeks gums tongue floor of the mouth or lips Subsequently patches of the hyperemic zone begin to resolve leaving a number of slightly raised discrete red *vesicles* which break down into small extremely painful *ulcers* resembling *aphthae* There i a submaxillary *lymphadenitis* and the temperature may rise 1 to 3 degrees The disea e is self limited and is inclined to resolve in two weeks or less

The herpetic virus (p 433) is probably the causal agent of this sto matitis although beta hemolytic streptococci which may be secondary invaders are recoverable by culture

Local treatment involves the daily application of 1 per cent Acriviolet Solution followed by Compound Tincture of Benzoin If pain is severe a solution of 3 to 10 per cent Ethyl Aminobenzoate (p 3114) is applied to sore spots directly before meal

APHTHOUS STOMATITIS

Aphthae may appear in any part of the mouth but are located most frequently in the folds of the lips and cheeks and under or on the edge of the tongue Like other herpetic disturbances they are recurrently pre cipitated by gastro intestinal disturbances and other irritants that alter tissue immunity

The aphtha generally appears singly as a small raised oval *vesicle* about 0.5 cm long surrounded by a bright red areola Within a few hours the vesicle ruptures leaving a sharply demarcated painful *erosion* covered by a pearly gray membrane and surrounded by an elevated red border Aphthae persist for a week to ten days regardless of treatment They must be differentiated from mucous patches drug eruptions and traumatic ulcers (p 1668) (See Fig 363)

The most effective method for controlling pain is to apply pure *phenol* to the ulcer followed immediately by *Compound Tincture of Benzoin* Silver nitrate which is commonly used is painful and ineffective

The presence of the lesion is sufficient to arouse the suspicion of an avitaminosis especially relative to the riboflavin portion of the B complex

Treatment—In addition to the measures used for the palliation of simple cheilitis the patient with the perleche should be given daily applications of 5 per cent zinc chloride followed by a dusting powder of zinc stearate Whole vitamin B complex is administered orally in large dosage and the riboflavin portion may be injected intravenously

SUPPURATIVE CHEILITIS

Furuncles and carbuncles of the upper lip are serious infections The disturbance initiates as a widespread area of induration it is accompanied by considerable pain and sublingual lymphadenitis Localization takes place slowly with pointing in the central area

Treatment—Suppurative cheilitis involving the upper lip must be handled with greatest delicacy since thrombophlebitis of the facial veins or cavernous sinusitis may be induced by squeezing or premature incision (p 1446) the area is poulticed with copious warm moist dressings of *boric acid* or a solution improvised by dissolving a tablet of 0 5 gm of *sulfadiazine* in one half glass of water Local application of *roentgen ray* may abort or hasten suppuration Anti infective therapy with sulfonamide (p 88) and/or *penicillin* (p 106) is necessitated for prevention and control of complications

NONSPECIFIC STOMATITIS

Inflammations of the mucous membranes of the oral cavity may be acute or chronic localized or diffuse mild or severe They may have only topical importance or they may be local manifestations of systemic disorders (p 1667)

The presence of a stomatitis becomes apparent when the patient complains of soreness of the mouth and the examiner notes redness edema vesiculation ulceration and a tendency toward bleeding

The significance of the stomatitis is determined best by the history associated conditions and bacteriological examinations Gonorrheal stomatitis actinomycosis thrush and trench mouth yield characteristic morphological findings on the stained smear (p 50) The lesions of the acute *eruptive disorders are associated with constitutional manifestations* particularly fever Metallic poisonings reveal deposits in the region of inflamed gums and the patient gives a history of occupational or drug contact with the offending substance The diabetic has a glycosuria (p 3673) and a hyperglycemia bleeding diatheses are revealed by the hemogram vitamin deficiency states are recognized by the history and the therapeutic response to multivitamin preparations

Treatment—The most important principle of treatment in nonspecific stomatitis is the *prevention* of further trauma A liquid or soft diet is prescribed cold foods are usually less irritating than hot the mouth is thoroughly rinsed after each feeding In infants retained food particles are removed digitally the finger of the attendant being protected by a rubber cot Pain is relieved by the *local application of 3 to 10 per cent ethyl aminobenzoate*

Potassium chlorate is often prescribed in doses of 0 2 to 0 6 gm (3 to

[illegible] manifestations [illegible]
[illegible]

The [illegible] (p. 30[illegible])

THRUSH

Thrush is a fungous infection of the mouth [illegible] in [illegible] but occasionally affects [illegible] It appears first on the tongue as [illegible] white, glistening patches which [illegible] the palate, buccal mucosa and pharynx. In the [illegible] stages [illegible] away. Lingual papillary atrophy may [illegible]

Diagnosis and Treatment.—Discovery of the Monilia albicans (p. 50) in material scraped from the lesions confirms the diagnosis. Resolution takes place under proper constitutional support, and the early application of a 1 per cent solution of [illegible]. Prognosis is unfavorable if lesions extend deeper into the respiratory or gastrointestinal tracts.

Prevention, in infants, is governed by attention to the hygiene of nursing. Bottles and nipples are vigorously boiled. The general nutrition is improved by diet therapy and the supplementary use of vitamins (p. 620).

ACTINOMYCOTIC STOMATITIS

Abscesses caused by actinomyces (p. 489) occur in the submaxillary region, cheek and tongue. Invasion probably takes place through the oral mucosa but the submaxillary and buccal types are first recognized by the appearance *of several nodules in the adjacent skin*. These slowly enlarge and involve the deep subcutaneous layers in a diffuse swelling. The lesion becomes indurated and sore, the skin is red and there is moderate trismus of the jaws. The gums opposite the swelling appear tender and *hypertrophied*. *Finally* the abscess becomes fluctuant and ruptures, discharging serous fluids or pus exhibiting *sulfur granules* which contain the ray fungus. The fistula thus established are characterized by a depressed orifice with a bluish areola. *Lingual actinomycosis* begins as a deep nodule *that enlarges slowly until it ruptures spontaneously* discharging characteristic pus.

Treatment.—Prior to the introduction of the anti-infective agents actinomycotic lesions were unsatisfactorily managed by increasing doses of *iodide (p. 492) and radical surgery. More promising results may be anticipated from the use of penicillin* (p. 111).

NOMA (CANCRUM ORIS)

Noma is an acute infectious disease occurring chiefly in institutionalized children following epidemics of *scarlet fever* (p. 1[illegible]1) or *measles* (p. 409). A second factor of predisposition is poor nutrition, probably a *deficiency of vitamin C* (p. 6[illegible]9). The exciting cause is invasion by the fusospiral group of oral organisms.

The onset is sudden and is marked by prostration and fever rising to 105° F. Initial oral symptoms are a characteristic putrid odor to the breath and the simultaneous appearance of dark indurated spots on the

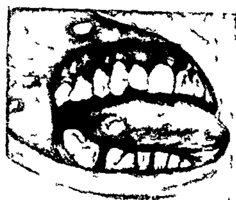


Fig 363 —Aphthous stomatitis due to staphylococcus infection *

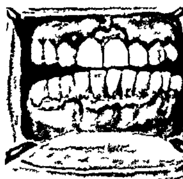


Fig 364 —Ulceromembranous gingivitis due to Vincent's infection *



Fig 365 —Perleche

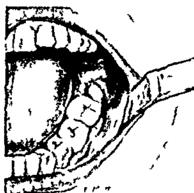


Fig 366 —Pericoronal abscess on partly erupted third molar *



Fig 367 —Black tongue lymphatic leukemia (C M Epstein)

GONORRHEAL STOMATITIS

Gonorrheal stomatitis is usually associated with *vaginitis* (p 2586) in young children The *diagnosis* is made bacteriologically since there are

* Thoma Oral Diagnosis

In *refractory cases* frequent applications of a thick watery suspension of zinc peroxide often bring rapid improvement Irritants and condiments tobacco and alcohol should be interdicted during the acute stages

Specific satisfactory results have been obtained both with sulfonamide (p 88) and penicillin (p 106) but local treatment as outlined above must not be neglected A daily dose of 4 gm of sulfathiazole given for 2 to 6 days has been reported to afford effective control though the results are by no means uniform By analogy to syphilis penicillin should prove of even greater efficacy whether given by intramuscular injection or top ical application If the anti infective agents prove unsuccessful intravenous injections of mapharsen merit trial

As the disease lapses into *chronicity* the patient should be referred to the dentist for thorough but cautious hygienic treatment This is directed at the foci or incubation zones that persist in the interdental crevices and under overhanging fillings and retromolar flaps The existence of these retards the final cure and invites recurrence The aftermath of the infec tion is a more or less extensive destruction of the crests of the alveolar

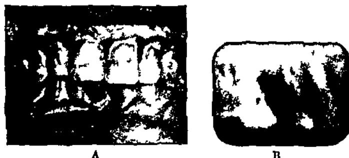


Fig 368—*A* Extragingival dental calculus deposited on the teeth *B* Subgingival calculus which is seen in roentgen film only

processes which often become a starting point for *pyorrhea alveolaris* (p 1700) Refractory infections may be encountered as the result of an underlying *blood dyscrasia* and a *hemogram* (p 3704) is required to clar ify the point

GINGIVITIS

The normal gums are pink and firm with festooning margins that are in close contact with the necks of the teeth A shallow crevice is produced by inversion of the gingivae just before insertion The interdental papil lae are V shaped projections of the gums they extend between the teeth and terminate in a slightly bulging apex at the point of contact of the teeth

The Formation of Tartar—An important factor in the production of gingivitis is the local irritation that results from formation of tartar *Cal cium salts* are precipitated from the saliva and they mix with the *lepto thrixes* and *actinomyces* that are normal inhabitants of the mouth A *dental calculus* formed at the cervical margins of the teeth exerts pres sure which causes eversion and irritation of the gingival margins Tartar

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posterior lower gums and the adjoining cheek tissue Necrosis spreads rapidly from these centers the gums and cheek swell and presently a red patch appears on the external cheek This is rapidly followed by extensive sloughing of the whole substance of the cheek In many cases the side of the nose and the pharynx are also involved The odor emanating from the wound becomes overpowering

The prognosis is extremely grave, the results of *treatment* depend largely on early recognition Intensive treatment with the anti infective agents is instituted using *sulfonamide* (p 88) and *penicillin* (p 106) by continuous intravenous drip Radical excision by cautery applications of zinc peroxide paste and supportive nutritional measures sometimes arrest the disease but leave extensive disfigurement

FUSOSPIROCHETAL STOMATITIS AND GINGIVITIS (TRENCH MOUTH)

Fusospirochetal infections (p 355) of the mouth may spread from a *Vincent s angina* or the sequence may be reversed More consistently however the condition is confined to the oral cavity

Clinical Manifestations—The disease has a predilection for patients in the late teens It begins as a generalized inflammation of the gum margins and small punched out *necrotizing ulcers* appear within a short time These involve the gum septa between the teeth the gum flaps covering partly erupted third molars and the floor of the mouth and buccal mucosa Characteristic *ulcers* are covered by a dirty gray slough they are moderately *painful and bleed easily (Fig 363)*

In the acute stage there is a slight elevation of temperature cervical lymphadenitis and a putrid odor to the breath

Etiology Diagnosis and Pathogenesis—Smears scraped from material under the sloughed films yield such a profusion of *Treponema vincenti* and *fusiform bacilli* as to obscure all other morphologic elements Stress is laid on the fact that these organisms probably playing the role of secondary invaders are recoverable as well from a host of nonspecific ulcers of the oral mucosa (p 1668) A positive smear alone cannot be accepted as diagnostic of Vincent s infection whereas a negative smear suggests an alternative diagnosis

At times there are endemic outbreaks of this disease (Trench mouth) and due attention should be paid to preventive treatment Predisposition to the infection seems to be associated with subvitaminosis particularly of factors of the vitamin B complex and vitamin C Supportive therapy advantageously may include moderate doses of niacin (100 mg daily) or whole vitamin B

Treatment—During the *acute stage* local treatment consists of frequent applications to ulcerated areas and gum margins of Methylene Blue or Gentian Violet followed by rinsings with a warm solution of Sodium Perborate An effective prescription is

℞		
	Crystal Violet	1 0
	Brilliant Green	1 0
	50 per cent Alcohol q s a d	100 0
	For local use	

exudate oozes into the pockets and precipitates a much darker harder and more adherent variety of deposit which provokes increased irritation At this stage food detritus and bacteria forced underneath the gum margin rupture the surface epithelium *pyogenic* or *fusospiral infection* of the exposed connective tissue occurs and pus is expressed from the gingival margins

DIFFERENTIAL DIAGNOSIS OF

Disturbances of the Gums

The mucous membranes of the gums are particularly vulnerable to local disturbances They may reflect also manifestations of profound systemic disorders

	DIAGNOSTIC FEATURES
Trauma	Ulceration and bleeding following extraction Traumatic gingivitis from misuse of toothbrush or dental floss
Local Inflammations	Simple and aphthous gingivitis Pyorrhea alveolaris Gum boil Ulceromembranous gingivitis (trench mouth) with Vincent organisms demonstrable by smear
Systemic Infections	Primary and secondary syphilis with positive darkfield microscopy and serology Actinomycosis with demonstrable ray fungi in scrapings from exudate (p 50)
Metabolic	Avitaminoses with therapeutic response to riboflavin and niacin Scurvy with therapeutic response to cevitamic acid Sprue with therapeutic response to vitamin B complex Diabetes mellitus with spongy gums and glycosuria
Allergy	Contact glossitis from dentifrice or mouth wash
Endocrinopathies	Hyperplastic gingivitis with epulis in association with pregnancy or administration of estrogen Bleeding in vicarious menstruation
Pharmacologic	Hyperplastic gingivitis with dilantin (p 1517) Pigmentary deposits in lead mercury and bismuth poisonings with identification of element in urine
Hematologic	Bleeding and hemorrhagic lesions in agranulocytosis thrombocytopenic purpura leukemia infectious mononucleosis polycythemia vera and aplastic anemia Note characteristic hemogram (p 3704) Hemorrhagic tendency in hemophilia with familial history

Acceleration of the pathologic process soon involves the entire peridental membrane As this membrane lies between the unyielding strata of tooth root and bone inflammation and thickening cause the tooth to protrude from its socket and become loose Separation and often extensive migration of the tooth take place unless the disease is arrested and recurrences promptly treated the tooth is lost

accumulates rapidly in the uncleaned mouth though careful hygiene does not completely prevent its formation in those who are more meticulous

The tartar varies from a white chalky deposit to a brownish grey variety of flinty hardness It is deposited in largest quantities opposite the orifices of the salivary glands the lingual surfaces of the lower anterior teeth and the buccal surfaces of the upper molars Long sustained pres sure *from the tartar deposits produces inflammatory changes of the* gums and edema of the interdental papillae The gums bleed easily and subsequently the crests of the alveolar processes resolve The gum mar gins lose their attachment to the necks of the teeth, a sulcus or pocket forms predisposing to the production of *pyorrhea alveolaris*

Clinical Manifestations —The clinical manifestations of gingivitis include *soreness and bleeding from the gums with the objective findings of puffi* ness deposition of tartar expression of pus from the crevices and in the chronic stages retraction of the mucous membrane The special vari

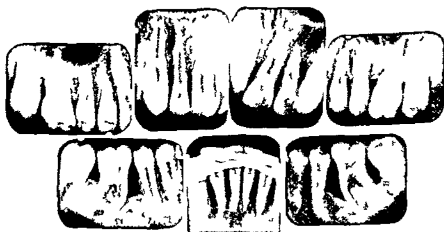


Fig 369 —X ray of periodontosis showing marked resorption of the alveolar bone in a boy 14 years of age

eties worthy of clinical recognition are hypertrophic inflammations and pyorrhea alveolaris (See Fig 368)

Hypertrophic Gingivitis —Hypertrophic gingivitis is most often a local *manifestation* of a systemic disturbance The gums become puffy and occasionally grow up over the teeth The condition is observed in *preg nancy* and following the use of *dilantin sodium* hypertrophy and puffiness of the gums with hemorrhage and ulceration is often a leading symptom in *acute leukemia* and *scurvy*

Pyorrhea Alveolaris (Periodontoclasia) —Pyorrhea alveolaris is an in evitable result of dental calculosis with its resultant inflammation Al though resolution of the gingivitis often restores an apparently healthy reattachment of the gum margins to the necks of the teeth the soft and bony tissues never completely regenerate In the course of time the gin givitis recurs and additional sectors of tissue are irrevocably lost The *subgingival pockets* increase in depth and extent and tartar becomes de posited deeply in these crevices as well as on the tooth surfaces Serous

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most desirable accuracy by roentgenograms which reveal also the condition of the dental pulp roots and periapical tissues

Prophylaxis and Treatment —The prevention and treatment of dental caries in the present state of our knowledge are best accomplished by local mechanical devices Little is to be anticipated from systemic therapy since the density of the tooth is modified by dietary and hormonal influences only during the developmental period A diet rich in *calcium* and *phosphorus* (p 678) supplemented by *vitamin D* may logically be expected to reduce the incidence of caries in children particularly if poorly soluble carbohydrates are eliminated In the adult elevation of a low blood calcium does not influence tooth structure or susceptibility to caries Conversely withdrawal of calcium from the formed enamel and dentin does not occur even in the serious disturbances of lime metabolism

DIFFERENTIAL DIAGNOSIS OF

Disturbances of the Teeth

While disturbances of the teeth are most often reflections of purely local abnormalities they may at times indicate profound metabolic or infectious derangement.

CAUSES	DIAGNOSTIC FEATURES
Congenital Anomalies	Supernumerary teeth delayed dentition and hypoplasia in achondroplasia and mongolism
Mechanical Disturbances	Malocclusion. Edentia Deposition of tartar Pulpitis
Local Disturbances	Recession of gums Abrasions and fractures Erosion Caries demonstrable by x ray
Metabolic Disturbances	Delayed dentition and hypoplasia in rickets *cretinism acromegaly avitaminoses and mal nutrition* Get B M R and note therapeutic response to administration of vitamins A and D and to thyroid extract. Mottled enamel in fluoride poisoning (p 1678)
Systemic Infections	Hutchinson s teeth in prenatal syphilis with positive serology (p 2787)
Chemical Disturbances	Staining due to neglect and nicotine Mottling in fluoride poisoning

Of academic interest but no present practical significance are the observations that *pantothenic acid* (p 626) in the saliva stimulates the production of the caries-producing lactobacilli *Fluorine* added to drinking water or locally applied in tablets containing vitamins C and D (Enziflur) decreases the incidence of caries of erupted permanent teeth (ages 8 to 13 years) Given before the age of eight fluorine may cause mottling (p 1678) and brittleness of the enamel

The prevention of dental caries is dependent upon frequent dental examinations and prompt treatment of lesions that are already *existent* The modern dentist realizes that ordinary inspection and exploration of the teeth often fail to disclose cavities in the unexposed surfaces He relies to an increasing extent on radiographs of these surfaces The prac

Diagnosis —The diagnosis of pyorrhea alveolaris is established by clinical signs and the disclosure of extensive atrophy of the alveolar process in dental roentgenograms Prognosis is generally favorable unless more than half of the tooth root has been deprived of its support

The purely localized forms of gingivitis must be distinguished from those which are manifestations of a widespread systemic disorder The presence of *pregnancy* or treatment with *dilantin sodium* clarify the origin of a hypertrophic gingivitis a *hemogram* (p 3704) is required for the recognition of a *blood dyscrasia* metal poisoning is suggested by the history, a contactual gingivitis is suspected when other causes are eliminated the importance of the vitamins is best determined by the *therapeutic test* particularly using the ingredients of the B and C complexes

Treatment —The *prophylaxis* of gingivitis requires removal of tartar by the dental hygienist During the stage of acute inflammation a soft or liquid cold diet is preferred The patient is urged to discontinue vigorous *tooth brushing and is advised to apply soap rather than a detergent* The prescription of an *amebacide* is based on the erroneous conception that pyorrhea is due to a specific organism *Astringent mouth washes*



Fig 370 —Bite wing films showing extensive dental caries

containing zinc chloride as the active ingredient are of some symptomatic value

DENTAL CARIES

Dental caries is a localized process of decalcification that invariably begins on the enamel surface Particles of food debris especially coarse carbohydrate material become wedged between the teeth or in the fissures of the biting surfaces Here they undergo *fermentation* as the result of the action of the oral aciduric micro organisms The acids that are formed dissolve inorganic enamel and dentin matrix and peptonize the organic residue of dentin Unchecked the carious process eventually reaches the dental pulp which responds to chemobacterial irritation by inflammation and putrescent necrosis Terminally the periapical tissues are involved to produce acute or chronic infection laying the foundation for a *septic focus* (p 1681) The rate of carious progress depends largely on the density of the hard structures of the tooth Those portions that have been calcified in utero are unusually resistant

Clinical Manifestations —Dental caries is best recognized by the specialist though the practitioner may have little difficulty in detecting large cavities in more obvious locations The condition is recognized with the

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bacteremia osteomyelitis of the jaw (p 1706) and respiratory embarrassment due to pressure on the airway

Chronic Granulomatous Periapical Abscess—A chronic granulomatous periapical abscess develops when the local tissue immunity is reasonably high and the virulence of the invading organism is feeble Most chronic abscesses are symptomless and they concern the practitioner principally as possible foci of infection (p 1681) They are recognized on radiographs

DIFFERENTIAL DIAGNOSIS OF

Disturbances of the Jaw

Abnormalities of the jaw may be of great complexity since they may involve osseous or articular structures muscle and lymphatic or salivary glands Fortunately the involved tissues are readily accessible to examination by palpation aspiration or biopsy

	DIAGNOSTIC FEATURES
Local Inflammations	Suppurative parotitis Dento-alveolar abscess Osteomyelitis of mandible or maxilla with demonstrable x ray changes (p 1706)
Systemic Infections	Epidemic parotitis Actinomycosis with *lumpy jaw and ray fungus demonstrable in* scrapings or exudate Mikulicz s disease with simultaneous involvement of lacrimal submaxillary and sublingual glands Sarcoidosis with uveitis Rabies with hydrophobia and history of dog bite Tetanus with lockjaw and history of penetrating wound
Mechanical Disturbances	Dislocations and subluxations of temporomandibular joint with inability to open or close mouth or with malocclusion Ankylosis of temporomandibular joint on congenital or acquired basis
Neoplasms	Benign or malignant tumors of parotid with definitive findings by biopsy Osteoma or sarcoma of mandible with positive x ray findings and biopsy Cysts of jaw with positive x ray findings and definitive histology by biopsy Adamantinoma (p 1714)
Metabolic Disturbances and Poisonings	Osteitis cystica fibrosa of hyperparathyroidism Prognathous in acromegaly Phossy jaw in phosphorus poisoning with history of occupational exposure Trismus in strychnine poisoning Sialolithiasis with x ray demonstration of calculi in salivary ducts Sialodochitis Osteomyelitis following radiation

alpha hemolytic streptococci are generally recovered in smears and cultures

Treatment—With the acute dento alveolar abscess premature surgical interference may result in the production of severe complications The patient is entitled to prophylactic treatment with sulfonamide (p 88) or penicillin (p 106) When the infectious process has become well localized it is cautiously incised and drained The tooth is most safely extracted *during the interval of remission* the socket is packed with sulfonamide

titioner should cooperate to the extent of urging frequent dental exam inations for his patient

The deciduous (milk) teeth are preserved until they are to be succeeded by the permanent dentition Unless this course is followed and the decid uous teeth are shed at the proper time malpositions and noneruptions of the permanent teeth are apt to result Since the period of great suscep-tibility to caries is the interval between early childhood and the late teens more frequent examinations are desirable at this time and the child is taught the importance of tooth brushing and dental prophylaxis

With the establishment of a cavity it is the function of the dentist to remove the necrotic areas and replace lost tissue with a metallic filling (p 1663)

PULPITIS

Pulpitis is a reaction of the dental pulp to irritating chemobacterial products resulting from dental caries or the physical irritation of a deep-seated filling The patient becomes aware of a sharp intermittent *pain* which is usually reflected to adjacent parts in such a manner as to make its origin difficult to elucidate The involved tooth is not tender to per cussion but contains a cavity or a large filling and is unusually sensitive to *cold* *Treatment* is the province of the dental surgeon The odontalgia of pulpitis is relieved by irrigating the carious cavity with a mild solution of bicarbonate of soda or by the insertion of a pledget of cotton saturated with Oil of Clove (p 3123)

PERICEMENTITIS

With any acute gingivitis trauma or a developing alveolar abscess the pericemental tissues become actively inflamed In contrast to pulpitis the pain is distinctly localized the tooth is tender to percussion and pain is aggravated by the application of *heat*

The pain of pericementitis is alleviated by cold applications and the use of a counterirritant such as iodine on the adjacent gums

DENTO ALVEOLAR ABSCESS

With progression of caries to the dental pulp the inflammatory proc ess may terminate in necrosis and infection The disturbance extends to the tissues immediately beyond the apex of the tooth the peridental mem brane and the spongy bone of the maxillae with eventual formation of a dento alveolar abscess of an acute or chronic variety

Acute Dento alveolar Abscess (Gum Boil)—An acute alveolar abscess re sults in the production of a large area of liquefaction and necrosis Pus burrows through bone and spreads laterally beneath the periosteum The acute abscess is symptomatized by a sudden onset with severe pain ten derness of the tooth on pressure more or less extensive swelling adjacent lymphadenitis and malaise (See Fig 366)

An acute abscess that involves the maxillary tooth generally localizes quite sharply One that involves a lower molar may be followed by several days of widespread and severe pain with massive indurated swelling The pus follows the fascial planes of the neck often pointing at a far distant site The possible complications of acute dento alveolar abscess include

bacteremia osteomyelitis of the jaw (p 1706) and respiratory embarrassment due to pressure on the airway

Chronic Granulomatous Periapical Abscess—A chronic granulomatous periapical abscess develops when the local tissue immunity is reasonably high and the virulence of the invading organism is feeble Most chronic abscesses are symptomless and they concern the practitioner principally as possible foci of infection (p 1681) They are recognized on radiographs

DIFFERENTIAL DIAGNOSIS OF

Disturbances of the Jaw

Abnormalities of the jaw may be of great complexity since they may involve osseous or articular structures muscle and lymphatic or salivary glands Fortunately the involved tissues are readily accessible to examination by palpation, aspiration or biopsy

	DIAGNOSTIC FEATURES
Local Inflammations	Suppurative parotitis Dento-alveolar abscess *Osteomyelitis of mandible or maxilla with* demonstrable x ray changes (p 1706)
Systemic Infections	Epidemic parotitis Actinomycosis with lumpy jaw and ray fungus demonstrable in scrapings or exudate Mikulicz s disease with simultaneous involvement of lacrimal submaxillary and sublingual glands Sarcoidosis with uveitis Rabies with hydrophobia and history of dog bite Tetanus with lockjaw and history of penetrating wound.
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powder or a packing saturated with penicillin (1 cc = 1000 units) and systemic chemotherapy is continued

The treatment of the chronic periapical abscess presents no great problem The tooth may be extracted or the offending root amputated

OSTEOMYELITIS

In the region of the oropharynx osteomyelitis may involve mandible maxilla or the alveolus

Osteomyelitis of the Mandible —The mandible has its chief nutrient supply through the *inferior dental artery* Obstructive inflammation of this vessel is produced by physical or chemical agents but most frequently it is a sequel to acute infection involving the alveolus of one of the lower molars or bicuspids In consequence the early symptoms of osteomyelitis of the mandible are identical with those of the acute spreading *alveolar abscess* (p 1703) The diagnosis is suspected when drainage from the incision fails to recede after a few days and the teeth in the involved region become tender to percussion



Fig 371 —Osteomyelitis diffuse involvement *

The *course of the disease* is similar to that of osteomyelitis in other bones A small or larger segment peripheral to the point of arterial obstruction becomes necrotic and eventually separates off as a *sequestrum* Coincidentally an *involucrum* is formed which assists in maintaining the continuity of the mandible

The *diagnosis* is supported by the demonstration of a denuded roughened bone which may be felt by the examining probe Sequestra are noted in the radiograph or are discharged from the wound *Treatment* is conservative with persistent chemotherapy using sulfonamide and/or penicillin until the sequestrum is fully detached and expelled

Osteomyelitis of the Maxilla —The cortical bone of the upper jaw is thinner and more vascular than in the mandible Hence the destructive extent of osteomyelitis is smaller and more superficial The clinical picture is similar to that of osteomyelitis of the mandible but the symptoms are milder *Treatment* is identical

Osteomyelitis of the Alveolus (Dry Socket) —A frequent complication of tooth extraction is that which results from circulatory failure in the tooth socket Excessive traumatism of the dense bony areas and secondary in

* Thoma in Pullen Medical Diagnosis

fection by fusospirochetes probably determine this reaction The symptoms consist of unremitting severe *post extraction pain* with the appearance of a socket that is devoid of a formed blood clot There is little swelling or involvement of the lymph nodes The condition is self limited and heals in about two weeks

Treatment consists of protecting the exposed bone surface with a surgical paste of sulfonamide or an analgesic ointment A satisfactory surgical paste is undernoted

Zinc Oxide	2 0
Sulfanilamide	0.5
Oil of Cloves q s to make a stiff paste	
S g Mix freshly for each dressing and pack into socket with cotton tipped applicator	

A wax of penicillin locally applied may be more satisfactory at lesser risk

GLOSSITIS

The majority of the inflammatory processes that involve the tongue represent local manifestations of systemic disturbances such as infections avitaminoses and blood dyscrasias (p 1085)

The more strictly localized inflammatory involvements of the tongue include abscess Moeller s glossitis glossitis rhomboidea mediana and the hairy tongue

Abscess of the Tongue —Purulent inflammation of the tongue is of rare occurrence It becomes manifest through the complaint of intense pain redness and swelling and fluctuation that is readily discernible by palpation

Treatment involves the local use of heat in order to favor localization *Prophylactic chemotherapy* with sulfonamide and/or penicillin is advisable incision and drainage may be required if the infection fails to resolve

Moeller s Glossitis —Moeller s glossitis is characterized by intense *burning* of the tip of the tongue The subjective complaint is soon followed by the development of intensely red denuded patches which appear at the tip or lateral border The areas are so tender that eating is extremely painful In contrast to riboflavin deficiency there is no accompanying cheilosis

Moeller s glossitis is usually a precursor of *primary hyperchromic anemia* (p 1077) but many patients fail to show the characteristic hemogram particularly in the early stages Remissions and recurrences of the symptoms may occur irrespective of treatment

The patient with Moeller s glossitis is entitled to a careful survey for evidences of the blood disturbance (p 3692) Local relief is afforded by the topical application of Ethyl Aminobenzoate in 3 to 10 per cent solution particularly before meals Concurrently a therapeutic test with liver extract (p 1048) and vitamin B complex (p 622) is well worth consideration

Glossitis Rhomboidea Mediana —Glossitis rhomboidea mediana is a rare condition which involves the midline of the dorsum of the tongue usually in its middle third The patient notes an almost bluish slightly indurated area which is smooth and shiny There are no objective symptoms the

powder or a packing saturated with penicillin (1 cc = 1000 units) and systemic chemotherapy is continued

The treatment of the chronic periapical abscess presents no great problem The tooth may be extracted or the offending root amputated

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* Thoma in Pullen Medical Diagnosis

Clinical Manifestations —Parotitis is rarely a metastatic infection It usually *results from food impaction* or *ascending* infection of Stenson s duct The condition becomes manifest as a painful swelling of the gland and is usually accompanied by constitutional manifestations of considerable severity The prognosis of complicating parotitis is most ominous but not completely hopeless

Treatment —The prevention of parotitis is accomplished by encouraging the flow of salivary secretion This is effected by having the conscious patient chew gum eat and drink Unconscious and enfeebled persons are

DIFFERENTIAL DIAGNOSIS OF

Ptyalism (Hypersalivation)

Hypersalivation may re ult from a wide variety of local and systemic disturbances It is to be differentiated from drooling which is due merely to deficiencies in the motor innervation of the muscles of the face

	DIAGNOSTIC FEATURES
Inflammatory	With stomatitis gingivitis glo sitis Ludwig s angina retropharyngeal absce s peritonsillar abscess pharyngitis and tonsillitis recognized by local inspection In ulceromembranous lesions with Vincent organisms demonstrable on smears (p 50)
Metabolic	In pregnancy scurvy and avitaminoses Note therapeutic responses to multi vitamin preparations
Chemical Disturbances	With mercury lead and bismuth poisonings and demonstrable elements in urine In iodism Following the use of cholinergens such as pilocarpine and physostigmine
Psychogenic	From stimulus of food With nausea and vomiting In hysteria and the various types of idiocy
Neurogenic	In facial palsy general paresis hydrophobia trigeminal neuralgia paralysis agitans bulbar palsy and epidemic encephalitis Supplement neurological findings with blood and spinal fluid serology and colloidal gold reaction

treated by gentle mouth washing oral irrigations and the application of mineral oil to the tongue and membrane

When parotitis develops efforts at oral hygiene are redoubled poultices are applied sulfonamides and/or penicillin are administered where facilities are available suppuration is encouraged by roentgen therapy The gland is gently milked in an attempt to favor drainage through the duct system As soon as fluctuation reveals itself surgical drainage is required taking special precautions to avoid injury to the facial nerve

MIKULICZ S DISEASE

Mikulicz s disease is a painless symmetrical enlargement of salivary and lacrimal glands due to hyperplasia of the lymphoid tissue Its onset

condition is benign in its course probably representing a terminal sclerosis of a chronic inflammation

No treatment is required

Hairy Tongue (Pigmented Hyperkeratosis of the Tongue) —The hairy tongue is the result of *keratosis* of the epithelium of the dorsum with large hypertrophic prolongations of the filiform papillae The condition becomes apparent from the appearance of the diffuse dark mass of intertwining hair like filaments containing deposits of decomposed blood which give rise to pigmentation The lesion is dark at the center and fades toward the periphery There are no subjective symptoms

The hairy tongue probably results from *prolonged local irritation* such as follows the protracted and intensive use of mouthwashes containing *sodium perborate* (p 1660) In the majority of cases discontinuance of the irritation brings about resolution of the lesion With persistence of the manifestations a solution of 5 per cent salicylic acid is applied to the filament several times daily followed by a rinse of hydrogen peroxide

See also Fig 367

LUDWIG S ANGINA

Ludwig s angina is an acute inflammation of the tissues of the *floor of the mouth* It is due to a bacterial invasion usually by *streptococci* The organisms enter an abrasion about the lower gums or in an infected socket of a lower molar tooth Occasionally the infection is secondary to *diphtheria* (p 302) or *scarlet fever* (p 171) Under these circumstances the path of invasion is between the mucous membrane and the periosteum of the lingual sides of the teeth Pathologically there is a widespread *cellulitis* but surgical exploration often uncovers a reservoir of pus above the level of the submaxillary salivary gland

Clinical Manifestations —Ludwig s angina begins under one side of the mandible as a red indurated swelling which spreads rapidly along the fascial planes of the neck until the entire inframandibular region is involved in an immense hard inflammation There is no tendency towards localization or fluctuation of the external swelling

Although the rise of temperature is generally moderate the patient appears extremely ill and cyanotic There is marked trismus the floor of the mouth is raised displacing the tongue upwards *Edema of the glottis* may be an early complication The prognosis is grave and hospitalization is indicated as soon as the diagnosis is suspected A tracheotomy set should be kept in readiness since *edema of the larynx* (p 2101) may develop

Diagnosis —Ludwig s angina is to be differentiated from the acute dental abscess which spreads along the floor of the mouth (p 1704)

Treatment —Early radical *surgery* is designed to relieve tissue tension Large supporting doses of *sulfadiazine* (p 88) and/or *penicillin* (p 106) are indicated before and after operation

PAROTITIS

Parotitis other than the epidemic variety in mumps (p 480) occurs in patients who have been immobilized comatose debilitated or helpless for a considerable length of time It results from neglect of dental hygiene and may be encountered during the use of an intravenous drip (p 3775) unless the mouth is kept moist and clean

CALCULOSIS OF THE SALIVARY GLANDS

Concretions or calculi occur frequently in the submaxillary glands or their ducts Calculi occur much less often in the *parotid* and rarely in the sublingual glands Stones are usually single irregular in shape and vary in size from that of a pinhead to a lima bean They lead to obstruction of



Fig 373—Salivary calculus in Wharton s duct In the periapical film the calculus is projected about the border of the mandible and may be mistaken for an area of osteogenesis The occlusal film reveals the true view and relations of the salivary calculus

the salivary flow and secondary infection which manifests itself by a circumscribed swelling in the vicinity of the gland and adjacent lymphadenitis Calculi are clearly demonstrable in well made roentgenograms (Fig 373) and lipiodol sialography (p 1658) is helpful in localization The *treatment* is surgical

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is insidious and after a course of several years it may recede spontaneously The swelling yields to roentgen therapy

A more frequently encountered syndrome resembling Mikulicz s disease is a unilateral hyperplasia of the lacrimal and salivary glands observed occasionally in such diverse conditions as iodide poisoning lymphatic leukemia and syphilis

CERVICAL LYMPHADENITIS

The submental sublingual submaxillary parotid postauricular and cervical lymph nodes may become tender or enlarged in the presence of inflamed infected or malignant lesions of the oropharynx The number of nodes involved and their location are often of assistance in differential diagnosis and may provide a clue to the position of the exciting lesion

The *submental and sublingual* nodes drain the lips the tip of the tongue the floor of the mouth and the lower incisor teeth



Fig 372—Mikulicz s disease *

The *submaxillary nodes are involved with lesions in the upper lip* the gums the lingual border and any of the teeth excepting the lower incisors

The *parotid* or *buccal* nodes drain the hard and soft palate and the gums overlying the upper posterior teeth

The *superior deep cervical* nodes drain the fauces and pharynx but may likewise but less frequently be coincidentally enlarged from lesions in any part of the mouth

The *inferior deep cervical* nodes drain the floor of the mouth and occasionally the tip of the tongue

Enlargement of many or all of the lymph nodes of the neck may take place without oral lesions as a manifestation of generalized or systemic *lymphadenopathy* (p 1136) Resolution of enlarged and tender nodes usually follows elimination of the cause Occasionally suppuration occurs and incision and drainage are required

* Major Physical Diagnosis



Fig. 3 4.—Mucous cyst of lips



Fig. 375.—Ranula formed from sublingual gland.*



Fig. 376.—Incisive canal cyst. All anterior teeth are entirely normal.†



Fig. 377.—Dentigerous cyst of the mandible involving the region from the first bicuspid to the first permanent molar in a boy nine years of age. Note displacement of the second bicuspid away from the line of occlusion.†

Thoma, Oral Diagnosis
† McCall and Wald, Clinical Dental Roentgenology

CHAPTER 86

CLINICAL DISTURBANCES OF THE OROPHARYNX: CYSTS AND NEOPLASMS

CYSTS

Oropharyngeal cysts are generally benign Some are of the retention variety such as *mucocele ranula* and *cysts of the incisive canal* A second type which includes *radicular coronal* and *dentigerous cysts* is derived from nests of paradental epithelial cells which proliferate under the stimulus of *caries pulpal inflammation and traumatism* The intermediate group of adamantinomas is derived from enamel forming cells (See Figs 376 377)

Adamantinoma (Ameloblastoma)—The adamantinoma is a tumor peculiar *to the jaw It is derived from embryonal enamel cells* and is found most frequently at the *angle of the mandible* of the middle aged

The adamantinoma begins as a slowly growing solid tumor invading the marrow spaces Subsequently it breaks down into numerous cystic compartments and distends the external plates of the jawbones thinning them so that they crepitate upon pressure The roentgenographic appearance closely resembles that of a dentigerous cyst even to the point of containing teeth Histopathologic examination may be required for differentiation (See Fig 378)

The primary adamantinoma is benign If it is removed incompletely it recurs rapidly infiltrates vigorously and metastasizes to the cervical nodes In the maxilla it invades the antrum defies total removal and is malignant

The *treatment of choice* in recurrent adamantinoma is surgical

well-circumscribed elevation varying in size from grapeseed to lima bean The surface is highly irregular resembling that of a sponge The papilloma is usually benign but may undergo malignant degeneration as a result of recurring traumatism

The papilloma should be removed by generous excision and cauterization of the base

FIBROMA OF THE GUMS

The fibroma of the gums is a slow growing pedunculated growth arising from the submucosa It is globular hard and painless and seldom attains a size larger than a filbert It is benign and requires no more than conservative excision and cauterization of the base A biopsy is required to exclude the possible presence of malignant degeneration

The *giant-cell fibroma of the gum generally follows* hypertrophic gingivitis of pregnancy (p 1701) It arises from the alveolar gum margin between the teeth and does not infiltrate bone It is a small oval purple



Fig 5 8—Monocystic adamantinoma of the mandible Note single cystic cavity which resembles the radicular or follicular cyst except that its outline is irregular and lobulated and its periphery is notched This has arisen from a radicular cyst

growth which is painless bleeds easily and grows slowly Complete excision often requires removal of adjacent teeth

ANGIOMA OF THE LIP

Nevi cavernous angiomas and lymphangiomas occur frequently on the *lips more commonly on the upper* Most are congenital and many are so extensive that the entire lip is enlarged (p 1685) Either single or multiple tumors may be observed in the form of firm purple lobular swellings of varying size Angiomas are benign and painless and *require* removal *for* cosmetic reasons by electrocoagulation

ANGIOMA OF THE TONGUE

Congenital hemangiomas of the tongue are painless lesions diffusely *distributed along its borders and dorsum* The *cavernous angioma* is cyan

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NEOPLASMS

The more common tumors of the oropharynx include fibromas osteomas angiomas lymphomas sarcomas papillomas adenomas carcinomas and mixed tumors Secondary tumors are rare but occur by extension from a growth in the nose or accessory sinuses or by metastasis from original lesions in the thyroid breast bronchi cervical lymph nodes or prostate gland

In addition to these neoplasms malignant degeneration may be observed in precancerous lesions such as keratoses fissures and ulcers Malignant degeneration is apparently stimulated by the chronic irritations of smoking jagged teeth impinging dental restorations oral sepsis chronic infection and highly spiced foods Because of the accessibility of the structures of the oral cavity it is a simple precaution to perform needle aspiration or punch biopsy in order to clarify diagnosis and crystallize indications for therapy

TABLE 120 — OROPHARYNGEAL CYSTS

Type	Location	Appearance	Treatment
Mucocele	Lip cheek or palate	Soft globular swellings with translucent cyanotic surface	Excision
Ranula	Floor of mouth	Painless swelling lateral to median line hemispherical and translucent with blue network of veins	Aspiration of fluid excision
Of Incisive Canal	Palate behind central incisors	Cystic degeneration of nasopalatine duct produces recurrent local swelling X ray shows circumscribed oval shadow beyond apices of incisors	Excision
Dento radicular Cyst	Pulpless teeth	Circular circumscribed shadows extending beyond apex of tooth root may cause local bulging of external plate of cortical bone	Extraction of tooth and enucleation of sac
Dentigerous Cysts (Dento coronal)	Crown of an unerupted tooth	In young patients x ray shows large irregular shadow containing one or more teeth (May destroy medullary bone and involve large area of jaw)	Excision and extraction
Adamantinoma	Angle of mandible	See text p 1719	Excision

Classification —Tumors of the mouth are most conveniently presented to the practitioner according to the site at which they occur However neither the location of the neoplasm nor its clinical appearance can be counted on to indicate the nature of the growth In any instance the final diagnosis should rest on histological examination of tissue

PAPILLOMA OF THE PALATE AND BUCCAL MUCOSA

Papillomas may occur on the buccal mucosa palate or tongue occasionally the tumors are multiple The appearance is that of a pallid oval

well-circumscribed elevation varying in size from grapeseed to lima bean The surface is highly irregular resembling that of a sponge The papilloma is usually benign but may undergo malignant degeneration as a result of recurring traumatism

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otic circumscribed and elevated beyond the dorsal or ventral surface, the *lymphangioma* is of the same color as the normal tongue, its contour is uneven and often cauliflowered

Angiomas are benign, removal by electrocoagulation is indicated for cosmetic or functional reasons

ADENOMA OF THE SALIVARY GLANDS

The adenoma of the salivary glands is a slowly growing solid and en capsulated tumor that generally invades only a small portion of the gland In pure form it is benign and yields to conservative surgery *Histologic study* is required to differentiate the neoplasm from a malignancy

DIFFERENTIAL DIAGNOSIS OF *Disturbances of the Palate*

Disturbances of the soft and hard palate are infrequently observed except as congenital abnormalities and manifestations of bulbar palsy

	DIAGNOSTIC FEATURES
Congenital Anomalies	Cleft palate and torus palatirus
Allergy	Angioneurotic edema of soft palate may cause obstruction to airway requiring scarification or local application of epinephrine
Infections	Diphtheria with membranous exudate and demonstrable organisms in smears and cul tures Primary and secondary syphilis with positive darkfield microscopy and/or serology
Neoplasms	Benign mixed and malignant lesions with defin itive histological recognition by biopsy
Neurogenic	Paralysis of soft palate with bulbar lesion par ticularly in diphtheria poliomyelitis and fol lowing cerebral vascular accidents
Psychogenic	Anesthesia and hypesthesia in hysteria

BENIGN TUMORS OF THE PHARYNX

Fibromas angiomas and papillomas may be observed on any portion of the pharynx Though benign they may spread rapidly to the fauces and nares causing difficulty in removal A *biopsy* is required to dispel the clin ical suspicion of malignancy

OSTEOMA OF THE JAWS

The osteoma of the jaws is found chiefly in the maxilla arising from the alveolar process beneath the antrum It grows slowly first filling the antral cavity then projecting through the nasal and external walls to produce a hard rounded smooth swelling in the infra malar region En tirely benign osteomas usually require only partial resection to relieve symptoms of pressure or deformity

MIXED TUMORS OF THE PALATE AND THE PAROTID AND SALIVARY GLANDS

The mixed tumor of the palate parotid or salivary glands is a complex growth which contains epithelial and mesoblastic tissue The tumor occurs most often in young adults Although its onset is sudden there follows a protracted quiescent period which may persist for twenty years At the end of this static stage growth may be resumed

The lesion is a *solid painless swelling* that usually involves only a portion of the affected structure As a rule it is encapsulated but it sometimes infiltrates through the substance of normal tissue to attain enormous size

Incomplete removal of the mixed tumor results in the acquisition of *malignant characteristics by the remnant Fortunately the residual tissue* is radiosensitive and postoperative roentgen therapy offers a favorable prognosis (See Fig 379)

EPITHELIOMA OF THE LIP

The epithelioma occurs chiefly in elderly males and has a predilection for the lower lip It is usually preceded by a chronic *keratosis* resulting from sharp teeth smoking or sunburn Persistence of a sore for months with subsequent scaling induration and erosion indicates a malignant tendency

The *papillary form* of labial epithelioma is relatively benign in the early stage and is flat superficial and hard It is usually situated to one side of the midline of the mucosal surface spreads slowly and after several months becomes ulcerated and painful Conservative surgery yields a high percentage of cures

The *ulcerative form* is far more malignant It may evolve from the papillary type but more typically *it begins as a small hard nodule* in the deep layers of the submucosa In either case it infiltrates the adjacent tissues rapidly and produces a characteristic oozing *ulcer* with a granular red surface and an uneven yellow indurated border (Fig 380) Later *the peripheral tissues become extremely inflamed and painful and* the submental and sublingual lymph nodes are involved At this stage the prognosis is grave but wide excision and radiation produce a small percentage of cures

LYMPHOSARCOMA OF THE GUMS

Lymphosarcomas may be primary on the gums occurring under overhanging fillings and poorly fitting bridges Small and sessile in the beginning *they have a soft easily ulcerating surface infiltrate rapidly into the* surrounding tissues and metastasize to the cervical lymph nodes Highly malignant they require radical surgery and appropriate radiation (Fig 381)

FIBROSARCOMA OF THE GUMS

Fibrosarcomas occur in young patients and spring from the alveolar periosteum They grow more rapidly than the pure fibrous type attain a larger size and are inclined to be sessile irregular in shape and have a purple tinge Long standing tumors assume characteristics of malignancy with pain ulceration infiltration of neighboring tissues and metastases Early and radical excision is indicated

CARCINOMA OF THE GUMS

Carcinoma of the gums is a degeneration of a chronic indolent sore It is a flat tumor with indurated raised edges It acquires a cauliflower surface spreads rapidly to invade the underlying bone loosens the teeth and soon invades the satellite lymph nodes It is extremely malignant and early radical surgery is indicated

EPIDERMOID CARCINOMA OF THE TONGUE

The epidermoid carcinoma of the tongue is the most frequent and probably the most malignant of oropharyngeal carcinomas It occurs predominantly in males after the fifth decade usually at the site of a kera-



Fig 379 —Mixed tumor of palate



Fig 380 —Epithelioma of lip



Fig 381 —Lymphosarcoma of gum

totic precancerous sore The initial clinical manifestation is a superficial ulcer with an indurated base which rapidly erodes deeply in the center and is surrounded by a hard rolled rim (Fig 382) Atypically it begins as a deep nodule which breaks down on the surface or as a benign papilloma which ulcerates to form the classic lesion The middle section of the lingual border is the most frequent location but it may appear on any part of the tongue Other sites of epidermoid carcinoma are the floor of the mouth buccal mucosa gums and pharyngeal wall

The carcinomatous ulcer spreads rapidly becomes secondarily infected and infiltrates the fauces floor of the mouth and mandible The dependent

lymph nodes are involved early frequently together with the correspond ing chain on the opposite side

Radiation is the *treatment* of choice and offers reasonable hope of cure in early cases The *prognosis* in later stages is extremely grave

LYMPHOSARCOMA OF THE PHARYNX

Lymphosarcoma appears primarily in the pharynx about as frequently as in the cervical nodes It begins on the wall or at the tonsillar ring as a *hard nodular swelling of the submucosa* It becomes superficial and occa sionally ulcerated and spreads rapidly to invade contiguous parts the cervical nodes and remote structures Surgery and radiation afford tem porary relief but recurrence is almost inevitable

CARCINOMA OF THE PHARYNX

Carcinoma of the pharynx is generally initiated in the peritonsillar region as the classic indurated ulcer with raised irregular margins It *spreads rapidly involves the lymph nodes* and has an early *fatal issue*



Fig 582 —Epidermoid carcinoma A very early lesion in the form of a small ulcer under the tongue with a glistening grayish surface

Pain which is a prominent symptom often resembles *Sluder's syndrome* (p 1482)

SARCOMA OF THE JAW

Sarcoma of the jaw occurs chiefly in children and arises from the periosteum of the midsection of the mandible the premaxilla a tooth socket or the antrum It invades and rapidly destroys the marrow spaces Often the first sign of disease is displaced and loosened teeth with fungat ing nodules around the cervical margins Radiographs of sarcomas show large circumscribed shadows invading the medulla and may be confused with *dentoradicular cysts* (p 1714) Successful *treatment* depends on rad ical *excision* inclusive of a large zone of uninvaded bone

CARCINOMA OF THE SALIVARY GLANDS

Carcinoma of the salivary glands occurs more frequently than the adenoma from which it may develop It is characterized by rapid growth *which early involves the entire gland and metastasizes* to the adjacent lymph nodes The prognosis is poor Roentgen therapy rather than sur gery is the treatment of choice

CHAPTER 87

CLINICAL DISTURBANCES OF THE ESOPHAGUS

ANATOMIC REVIEW

See p 3559

PHYSIOLOGY

Air Swallowing (Aerophagia) —Fluoroscopy of the esophagus reveals the frequency and extent of aerophagia Most individuals swallow a certain amount of air with the bolus of food others take in large quantities of atmospheric air without reference to food and then release an audible and satisfying belch Some of the swallowed air is trapped in the stomach to produce the *air bubble* or *magenblase* Contrary to general opinion this disengorged gas is atmospheric air and not a product of gastric fermentation or decomposition

Intra esophageal Pressure —The esophagus is closed at its upper end by the cricopharyngeal muscle and at its lower end by the pinchcock action of the diaphragm As a result the pressure within the esophagus is *negative* with reference to atmospheric pressure and measures approximately 3 to 5 mm of Hg Its extent is determined by the pressure within the mediastinum which in its turn is conditioned by intrapleural pressure With decreased intrapleural pressure and weakness of the esophageal walls large amounts of atmospheric air are trapped in the esophagus

Swallowing —The process of *deglutition* ends with discharge of the bolus of food into the upper end of the esophagus where the crico pharyngeus muscle relaxes to receive it The *descent of food* through the upper two thirds of the esophagus is extremely rapid and is dependent mostly upon gravity However the esophagus is not a passive conductor of food from mouth to stomach a *peristaltic wave* seen during fluoroscopy lags behind the bolus in the upper portion of the gullet catches up with the food masses at the cardia and transfers it actively to the gastric lumen *Retroperistalsis* which occurs in normal individuals is seen almost universally in obstructive conditions involving the gullet

SPECIAL METHODS OF EXAMINATION

Ordinary methods of physical examination are of limited value in investigation of the esophagus Palpation in the neck may reveal the presence of retained food in a *large diverticulum* (p 1730) a *metastatic lymph node* may be felt in the supraclavicular region

Roentgenography —For definitive information concerning the gullet the patient must be referred for radiographic study Contrast is afforded by the use of a *thick barium mixture* Small lesions particularly those of a malignant nature are often not demonstrable by roentgenography even when quite apparent by esophagoscopy



Fig. 383 —Anter or d splacement of the esophagus by r ght aortic arch Also not di erti ula



Fig 384 —Displacement of the esophagus by massive l ft auricle

Buckst n Cl n cal Roentgenol gy of the Al mentary Tract

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Circulatory	From pressure due to aneurysm of aortic arch or congenital anomaly of right subclavian artery producing dysphagia lusoria Outline cardiac silhouette by fluoroscopy and barium meal

Esophagoscopy —Direct examination with the esophagoscope is usually performed by the laryngologist Instrumentation of the esophagus is not without danger Particularly in the presence of gross pathological change *perforation* may occur often with fatal consequences The relaxation produced by curare (p 3888) makes esophagoscopy an easier and safer technical procedure

SPECIAL METHODS OF TREATMENT

Dilatation —Organic strictures of the esophagus are treated by special *esophageal dilators* This type of instrumentation is hazardous unless controlled by esophagoscopy It is the province of the specialist with unusual *technical experience*

Surgery —The surgical treatment of esophageal lesions is exacting and dangerous Penetrations and perforations require drainage of the mediastinal regions when infections occur or pressure symptoms threaten the vital structures in the neck Removal of a diverticulum is rarely necessary and should be avoided since the procedure is formidable and the risk great

Esophagectomy —Esophagectomy is performed by transpleural approach to the posterior mediastinum through an opening made in the left posterior chest wall The esophagus is dissected free and the involved segment is excised If a lesion is in the distal quarter or third of the esophagus the remaining portion of the esophagus often can be anastomosed to the fundus of the stomach which is brought up through an opening in the diaphragm If the carcinoma is higher up in the esophagus the proximal stump of the esophagus is brought up through the neck as an external esophagostomy At the same time or as a preliminary procedure a gastrostomy is made After healing esophagostomy and gastrostomy are connected by a rubber tube or a plastic skin tube along the anterior chest wall

The *operative risk* is quite high The patient is almost always emaciated and dehydrated nutrition must be improved before operation with the aid of preliminary gastrostomy or jejunostomy Frequent *postoperative complications* include pulmonary infection pleural effusion or pneumothorax

CLINICAL DISTURBANCES INVOLVING THE ESOPHAGUS

Because of its sheltered position the esophagus is rarely the site of *clinical abnormalities* Those most frequently encountered are local responses to systemic disturbances less often local lesions occur with or without systemic sequels They are listed below under their proper classifications

DIFFERENTIAL DIAGNOSIS OF

Dysphagia and Pain on Swallowing

The act of swallowing is a complicated neuromuscular reaction controlled by a central mechanism located in the vicinity of the vagal nuclei Deglutition is accomplished in three stages In the first phase under voluntary control the bolus is rolled backward toward the base of the tongue after which it is propelled with considerable force into the pharynx In the second phase food is guided into the esophagus avoiding forward movement into the mouth upward movement into the nasopharynx and forward and downward movement into the larynx and lower air passages The final stage of deglutition consists in propulsion of food, by peristalsis along the course of the esophagus and through the cardiac sphincter

In addition to pain on swallowing disturbances of deglutition may give rise to difficulties (dysphagia) including spitting of food, regurgitation through the nose and choking as the result of entrance into the airway Spitting of food is ordinarily a characterological or psychogenic manifestation It occurs particularly in infancy and in the major psychoses (p 1364) Regurgitation through the nose occurs most often with bulbar palsy as seen particularly in diphtheria poliomyelitis and following cerebrovascular accidents Entrance of food into the larynx ordinarily produces choking but should aspiration occur the patient may develop a pneumonitis or a lung abscess (p 2214)

	DIAGNOSTIC FEATURES
Congenital Anomalies	Cleft palate esophago-tracheal fistula atresia or webs demonstrable by esophagoscopy Diverticula outlined by x ray after swallowing thick barium mixture
Physical and Chemical Injuries	Foreign bodies removed by esophagoscopy Acute chemical burns with late stricture formation Traction diverticula demonstrable by x ray after swallowing thick barium mixture
Allergy	Angioneurotic edema relieved by epinephrine spray pyribenzamine (p 505) or scarification
Psychogenic	Globus hystericus without demonstrable lesion Cardiospasm with dilatation of esophagus by x ray Plummer Vinson syndrome with glossitis and low B M R
Neurogenic	Hydrophobia following dog bite Lockjaw with tetanus Regurgitation and choking following epidemic and other types of encephalitis encephalopathies and cerebrovascular accidents involving bulbar regions Supplement neurological findings with examinations of cerebrospinal fluid (p 3734)
Muscular	Inability to swallow in myasthenia gravis with therapeutic response to neostigmine (p 2880)
Local Inflammations	Esophagitis decubitus and peptic ulcers demonstrable by esophagoscopy Difficulty in swallowing with pharyngitis tonsillitis laryngitis glossitis Ludwig s angina epidemic parotitis and retropharyngeal and peritonsillar abscesses observable by direct inspection
Neoplasms	Benign and malignant growths demonstrable by esophagoscopy and biopsy (p 1723) With carcinoma of the gastric cardia From pressure due to mediastinal neoplasm

than fluids in contradistinction to the condition that prevails in malignancy

The *onset of symptoms* may or may not be related to an obvious emotional upset but the occurrence of the disturbance produces a dramatic emotional overplay the patient usually develops a panic state under the belief that she is choking to death

With a large dilatation of the esophagus *pulmonary symptoms* such as *cough* and *dyspnea* occur because of pressure With anatomic complications nutritional disturbances arise as in the Plummer Vinson syndrome

Ordinary physical examination throws no light on the disturbances of cardiospasm Instrumentation even the passing of the ordinary stomach tube is hazardous since a false passage and perforation may be produced



Fig 385 —Cardiospasm with tortuous esophagus

Specialist Examinations —*Roentgenography* during an attack reveals the hour glass appearance that is characteristic of cardiospasm the esophagus proximal to the dilatation may be distended to accommodate as much as a liter of fluid and suggests the presence of a mediastinal tumor Since spasm may be superimposed upon an ulcerating lesion such as carcinoma a positive diagnosis can be assured only by *esophagoscopy* (p 1723) In advanced lesions with a tortuous esophagus the passage of the scope is technically difficult

Diagnosis —Before the diagnosis of cardiospasm is definitively accepted the presence of an associated organic lesion such as neoplasm must be investigated Generally the patient with cardiospasm is a young woman rarely beyond the age of thirty five years carcinoma is a disease of males

Buckstein Clinical Roentgenology of the Alimentary Tract

LOCAL MANIFESTATIONS OF SYSTEMIC DISORDERS

Cardiospasm
Plummer Vinson Syndrome
Esophageal Varices
Esophageal Telangiectases

LOCAL LESIONS WITH OR WITHOUT SYSTEMIC MANIFESTATIONS

Congenital Malformations

Esophagotracheal Fistula
Absence or Obliteration
Narrowing and Webs
Diverticula (Zenker)
Short Esophagus

Mechanical Physical and Chemical Disturbances

Obstruction by Foreign Bodies
Laceration Perforation Penetration and Rupture
Injury from Instrumentation
Irradiation Burns
Traction Diverticula
Diaphragmatic Hernia (p 1803)
Strictures
Chemical Burns

Inflammations

Peptic Esophagitis and Peptic Ulcer of Esophagus
Decubitus Esophagitis
Secondary Esophagitis

Neoplasms

Benign Neoplasms
Carcinoma of Esophagus

CARDIOSPASM (ACHALASIA)

Cardiospasm is generally a *psychosomatic condition* (p 1344) resulting from a profound emotional disturbance It may arise also as a reflex in patients with organic lesions of esophagus stomach or gallbladder

Pathogenesis—Although cardiospasm is commonly believed to be the result of *hypertrophy of the circular muscle* situated at the junction of esophagus and stomach, anatomic investigation does not reveal a true sphincter The funnel produced in cardiospasm occupies a position at the site of the esophageal opening in the diaphragm suggesting that the initial muscular disturbance involves the fibers of the diaphragm rather than those of gullet proper It is also possible that the disturbance is not the result of obstruction but occurs from an achalasia a derangement of the orderly peristaltic sequence the cardia fails to open when the wave which descends the length of the esophagus reaches the lowest third food becomes lodged above the cardia the lumen dilates and the concentric layer of smooth muscle undergoes hypertrophy

Secondary Pathologic Changes—Whatever mechanism initiates cardiospasm the esophagus sooner or later becomes dilated and tortuous the lower end of the gullet is funnel shaped and the lowest point of the funnel appears at the level of the diaphragm suggesting the operation of an extrinsic mechanism In the more prolonged examples the funnel descends below the diaphragm and may be at the level of the cardiac orifice

Associated with the changes in the lumen of the organ the muscular layers undergo *hypertrophy* and may approximate ⅛ inch in the thickness food particles are retained causing reddening edema and *ulceration* of the mucous membranes simulating malignancy *to the point* where a differential diagnosis can only be established by the histologic *examination* of a section of tissue obtained by *esophagoscopy* (p 1723)

Clinical Manifestations—Cardiospasm occurs more frequently in the *female* and the disturbance is noted typically but not exclusively in *young persons* The patient complains of *substernal discomfort* and a *sticking sensation* localized in the pharynx (globus hystericus) retrosternal or epigastric regions There is inability to swallow food or even fluids during meals or independent of feedings solids often pass down with greater ease

ship between demonstrable emotional or situational conflicts and the production of the symptoms Usually as can readily be understood the disturbance in food acquisition represents a frustration in the psychosexual sphere

Pharmacotherapy—Sedatives hypnotics and antispasmodics are combined in the drug therapy of cardiospasm *Antispasmodics* (p 2029) rarely accomplish much of therapeutic value the suggested drugs include nitrites (p 3892) which directly depress smooth muscle depressants of the cholinergic system including belladonna (p 3873) atropine and the newer synthetics such as syntropan and novatropine (p 3873) and demerol (p 3863) The ephemeral *nitrite* effect is of use only in an acute crisis the *belladonna* derivatives are given in full physiologic doses depending upon the individual reaction thus Tincture of Belladonna is started in 10 or 15 drop dosage and repeated at four hour intervals in increasing amounts until the mouth becomes uncomfortably dry *atropine* 1 mg ($1/60$ grain) *novatropine* 2 mg ($1/30$ grain) and *syntropan* 50 mg ($5/6$ grain) are given similarly Of the anti histamine agents pyribenzamine (p 56[illegible]) in doses of 50 to 100 mg may prove valuable particularly if repeated every two or three hours for at least four doses

A prescription that combines sedative and smooth muscle features is undernoted

Sodium Phenobarbital	0.25
Atropine Sulphate	0.012
Lactose q.s	
Divide and make 15 capsules	
Sig 1 capsule every 3 hours as directed	

Mistura Nigra (p 1757) is often most efficacious

In acute crises when the spasm is so intense as to demand immediate relief *demerol* (50 to 100 mg) may be given subcutaneously or *papaverin hydrochloride* in 60 to 120 mg (1 to 2 grain) dosage is injected intravenously Morphine dilaudid and codeine are avoided since they tend to increase spasm and produce addiction in psychoneurotic patients

Instrumentation—Instrumental treatment of cardiospasm as recommended by the gastro enterologists calls for the passage of a dilator or a *weighted tube* (p 1723) the patient is trained to pass the latter before each meal After some little experience most sufferers are able to maintain the patency of the esophagus for the entire duration of a meal Later it may be possible to reduce the use of the tube to once daily At times the more fortunate patient is able to discontinue the passage of the tube without experiencing a recurrence of symptoms

The dilator is best passed through the esophagoscope and inflated to a pressure of fifteen pounds

Surgery—Surgical intervention is considered when there are profound nutritional disorders In more advanced instances in which anatomic changes have occurred at the lower end of the esophagus it becomes increasingly difficult and dangerous to pass the tube Other dilating devices are similarly contraindicated because of the hazard Under these circumstances rarely encountered the surgeon is consulted relative to the possibility of operative intervention resection of the *sympathetic nerve sup*

usually beyond the age of forty The patient with cardiospasm frequently presents other evidences of the fundamental neurosis There may be emotional instability labile vasomotor responses with flushing blushing cold and clammy hands and feet tachycardia and other spasmodic phenomena such as attacks of diarrhea or spastic constipation In contrast the carcinomatous individual is generally older and more stabilized without manifestations of *autonomic imbalance* (p 1395)

The history of local symptoms in the patient with cardiospasm is frequently one of intermittence but in the carcinomatous individual the complaints are persistent with increasing severity though there are occasional remissions due to ulceration of the tumor The stool should be examined for occult blood which when present suggests the organic lesion

Course—The course of cardiospasm is variable The disturbance may rapidly disappear never to return More frequently however it is persistent or recurrent The perpetuation of the symptoms eventually results in organic change with dilatation of the lumen, hypertrophy of the muscularis retention of food and ulceration With these anatomic variations new symptoms appear such as regurgitation of food reflex cough hiccough or palpitation the latter dependent upon irritation of structures in anatomical relationship Eventually the patient fears to eat adding to the severity of the syndrome Evidences of malnutrition and deficiency states are superimposed as in the Plummer Vinson syndrome next to be described

Treatment of Cardiospasm—The management of cardiospasm combines psychotherapy drugs instrumentation and surgery Psychotherapy in our experience, has usually yielded sufficiently satisfactory results to preclude the necessity for employing mechanical forms of treatment It is our belief that intubation is physiologically and psychologically an unsound procedure Reference to the specialist is reserved for the few patients who develop secondary pathologic and metabolic complications After diagnostic esophagoscopy instrumentation is thoroughly tried before resort to surgery

Psychotherapy—It is our practice to stress psychotherapy in individual treatment *Formal psychotherapy* (p 1327) yields no better results than may be expected by routine methods Psychoanalysis (p 1325) is protracted and expensive

The patient is given complete assurance that the condition is benign and thoroughly understandable, she is told that her nutrition should not suffer that she will not choke or starve to death that it is unlikely that any consequences will attend the condition other than discomfort At the same time, she is warned that recurrences are the rule and to be expected and she is asked to return for further treatment If the practitioner does not consider it wise to state that the purpose of future visits is investigation into characterological and situational circumstances it is justifiable to employ the subterfuge of ordering hypodermic injections of one sort or another The conversations are then seemingly casual and incidental At subsequent visits the patient is asked to give a chronological history of her way of life (p 3473) If this proves too time consuming a diary history (p 3474) is requested

When the confidence of the patient has been established and the element of fear dissipated the practitioner attempts to explain the relation

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The dilator is best passed through the esophagoscope and inflated to a pressure of fifteen pounds

Surgery—Surgical intervention is considered when there are profound nutritional disorders In more advanced instances in which anatomic changes have occurred at the lower end of the esophagus it becomes increasingly difficult and dangerous to pass the tube Other dilating devices are similarly contraindicated because of the hazard Under these circumstances rarely encountered the surgeon is consulted relative to the possibility of operative intervention resection of the *sympathetic nerve sup*

ply to the lower end of the gullet has been attempted with some promise of success, a plastic resection of the *intra abdominal portion of the esophagus* has also proved of value in an occasional instance

PLUMMER VINSON SYNDROME

The Plummer Vinson syndrome is probably a later stage of cardiospasm (p 1725) to which a nutritional disturbance has been added

Clinical Manifestations—The Plummer Vinson syndrome occurs in women with nervous and emotional instability The *early symptoms* consist of choking spells during swallowing The patient becomes fearful of eating and discontinues adequate feedings A large amount of weight is lost, asthenia and emaciation are noted

Examination reveals a red atrophic and dry *tongue* associated with redness of the *mucous membranes* of the mouth The appearance of the tongue is that of deficiency of niacin (p 625) The *lips* have cracks fissures or rhagades (p 1676), suggestive of riboflavin avitaminosis *The basal metabolic rate* is quite surprisingly depressed (—20 to —30 per cent)

Laboratory examinations show a marked *secondary anemia* with a *gastric achlorhydria* (p 3725) *Esophagoscopy* fails to reveal any evidence of malignancy X rays may reveal an anterior indentation with proximal dilatation

Diagnosis—The Plummer Vinson syndrome is easily confused with *hyper chromic anemia* (p 1077) *symptomatic avitaminoses* (p 616) and *carcinoma of the esophagus* (p 1738) The character of the anemia is revealed by the *blood count* (p 3696) the suspicion of a malignancy can be allayed only by *esophagoscopy*

Treatment—The establishment of the diagnosis of Plummer Vinson syndrome often rests upon the *therapeutic test* The patient should respond rapidly to the *administration of iron* (p 1048) and *crude vitamin B complex* (p 622) In addition to measures aimed at correction of the digestive metabolic and hematologic disorders the patient is subjected to the routine used in the management of *cardiospasm* (p 1726)

ESOPHAGEAL VARICES

Esophageal varices develop when there is hypertension or obstruction *of the portal circulation (p 1960) The veins at the lower end of the esoph*agus and the cardiac end of the stomach (p 3560) anastomose freely and tend to shunt blood from the intestinal tract back to the heart without traversing the liver This anastomosis constitutes a safety valve in *portal obstruction*

Pathogenesis—With extensive hepatic obstruction such as occurs in *cirrhosis of the liver* and in the *Banti syndrome* (splenomegalic cirrhosis) the flow of blood from the portal vein is impeded and diverted by way of the esophageal veins, directly to the right heart These veins do not contain valves They support the weight of a large column of blood *in* the erect position thus increasing the pressure on their thin walls resulting in dilatation of the lumen tortuousness and varicosity

Clinical Manifestations—Esophageal varices do not give rise to symptoms until they bleed Persistent oozing produces a *secondary anemia* (p

1089) abrupt hemorrhage results in a *hematemesis* (p 1764) or a *gross melena* (p 1843)

Diagnosis—Because of the associated symptoms due to the advanced hepatic condition the diagnosis of bleeding from an esophageal varix is rarely difficult

Prognosis—With esophageal varices the outlook for the patient is exceedingly poor Dilatation of the veins does not occur until the hepatic function has been severely impaired



Fig 886—Varices of esophagus *

Treatment—Treatment is aimed at compensating for blood loss *anti coagulants* (p 1045) are of little if any value injection of the varices with *sclerosing solution* by way of the esophagoscope is a palliative procedure to be performed only by the specialist Anastomosis of the portal vein and the inferior vena cava may improve liver function and prevent further bleeding or accumulation of ascites

* Buckstein, Clinical Roentgenology of the Alimentary Tract.

ESOPHAGEAL TELANGIECTASES

Esophageal bleedings may emanate from telangiectases Under these conditions there is usually a *hereditary telangiectasia* (p 1119), recognizable by similar lesions of visible cutaneous or mucosal surfaces particularly within the mouth

The *prognosis* of these bleedings is not ominous *Cauterization* may be attempted through the esophagoscope

CONGENITAL ESOPHAGOTRACHEAL FISTULA

The esophagotracheal fistula is recognizable at birth The child *strangles chokes* and *coughs* on attempted feedings Unless the condition is recognized and tube feedings are instituted the infant dies within a few days as the result of aspiration of food If life can be maintained by tube feeding surgical therapy by an expert thoracic surgeon has a remote chance for correction of the defect provided that no other congenital lesions are present

CONGENITAL ABSENCE OR OBLITERATION OF ESOPHAGUS

Absence or obliteration of the esophagus is not compatible with life unless *feeding gastrostomy* (p 1759) *is rapidly performed and there are* no other congenital lesions Since abnormalities of congenital origin are usually multiple and the child has little chance of surviving the operative procedure the prognosis is exceedingly grave

CONGENITAL NARROWING AND WEBS OF ESOPHAGUS

Congenital narrowing and congenital webs of the esophagus interfere with deglutition and may cause total obstruction If recognized by diagnostic esophagoscopy or lipiodol injection of the esophagus the constriction may be *dilated* instrumentally and the web dissipated through an operating *bronchoscope* or *esophagoscope* (p 1723)

CONGENITAL DIVERTICULA (ZENKER)

Congenital diverticula of the esophagus usually occur at the junction *of pharynx and esophagus These defects are due to a* herniation of the esophageal mucosa through a gap in the upper gullet The sac usually lies between the circular and oblique fibers of the anterior pharyngeal constrictors

Clinical Manifestations—Congenital diverticula are of the *pulsion type* due to increased intra esophageal pressure *Food accumulates in them* in considerable quantity and they may be the cause of *throat irritation dysphagia* (p 1722) *regurgitation* or *obstruction* At times congenital diverticula of the esophagus produce a prominent visible or palpable *tumor* in the neck The intrathoracic diverticula are not diagnosable except by radiography

Diagnosis—Because of ulceration and obstruction secondary to irritation and inflammation of the sac esophageal diverticula often simulate *cancer* of the gullet, differentiation is only possible as the result of diagnostic *esophagoscopy* (p 1723) *Traction diverticula* (p 1734) occur at the level of the bifurcation of the trachea and are usually secondary to healed tuberculous glands demonstrable radiographically

Radiography—On suspicion of the presence of an esophageal diverticulum the patient is given a thick barium mixture The esophagus is examined in all planes under which circumstance the sac is usually demonstrable

On many occasions the esophageal diverticulum is a chance finding during a gastro intestinal radiography Unless symptoms pointing to retention or ulceration of the sac are present therapy is not indicated

Treatment—In the presence of symptoms arising from the congenital disorder an attempt should be made to discover a position in which the diverticulum spontaneously empties itself into the lumen of the gullet proper If this can be accomplished every effort should be made to avoid



Fig 387—Zenker diverticulum

surgical intervention since the operative procedure is often much more formidable than originally suspected

CONGENITALLY SHORT ESOPHAGUS

The congenitally short esophagus varies in degree The gullet may be so abbreviated as not to extend below the third rib More often the shortening is not excessive and the esophagus reaches to within 1 to 2 inches of the hiatus of the diaphragm

Clinical Manifestations—The congenitally short esophagus usually goes unnoted and produces no *symptoms* The diagnosis is made by chance in the conduct of a gastro intestinal radiography for some other purpose In other instances as the result of the esophageal shortening a variable portion of the stomach is drawn through the diaphragmatic opening produc

ing a clinical picture resembling *para esophageal* or *diaphragmatic herniation* (p 1803)

Symptoms caused by the short esophagus rarely appear until the patient reaches middle life There may be low *substernal pain* radiating to the left shoulder and arm resembling *angina pectoris* (p 890) or gastric symptoms identical with those of *peptic ulceration* (p 1780) In the latter instance *hematemesis* not infrequently occurs further obscuring the clinical picture

Diagnosis—The diagnosis of short esophagus is not possible without radiography or esophagoscopy

Treatment—The treatment of symptoms arising from the short esophagus is most unsatisfactory An abdominal girdle or corset may be fitted



Fig 388—Thoracic stomach with short esophagus*

to force upwards abdominal contents and diaphragm thus relieving pressure on the herniated portion of the stomach With ulceration in the sac the usual peptic ulcer regimen (p 1790) is employed but the outcome is rarely satisfactory

With persistence of symptoms and especially in the presence of hematemesis the surgeon is consulted in the hope that it may be possible to achieve a corrective procedure A *left phrenicectomy* has been attempted with the idea of elevating the left leaf of the diaphragm and relieving tension on the intrathoracic portion of the stomach *Intra-abdominal and transthoracic approaches* to the problem are fraught with danger but give some promise of success In consequence none of these radical surgical

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procedures should be attempted unless all conservative methods have been exhausted and urgent symptoms persist

OBSTRUCTION BY FOREIGN BODIES

Foreign bodies may obstruct the esophagus Children swallow the tops of bottles large marbles coins and stones producing esophageal obstruction that may require removal by esophagoscopy

Foreign body obstruction results from ingestion of hydrophilic laxatives (p 1827) When the desiccated granules while still in the lumen of the esophagus become swollen with ingested water they may block the lumen so completely as to be removable only by esophagoscopy (p 1723) To prevent this occurrence patients are warned to lubricate the esophagus by the ingestion of water before swallowing the granules the second glass of water is not taken until the granules have had abundant opportunity to pass the cardia

LACERATION PERFORATION PENETRATION OR RUPTURE

Laceration perforation or penetration of the esophagus results from the swallowing of a chicken bone a fish bone or a piece of tin from a can *Spontaneous perforations* have been observed on rare occasions Seamstresses or carpenters holding pins or nails in their mouths sometimes swallow the foreign bodies Occasionally mentally unbalanced people and young children may swallow odd objects A pre existing partially occlusive but asymptomatic lesion of the esophagus may predispose to blocking

The patient immediately notices *dysphagia* and *substernal pain* In the vast majority of instances the discomfort is temporary since only the mucous membrane has been torn and the foreign body has not become impacted Under these circumstances the practitioner is rarely consulted However if the pain continues and increases the lesion may be of considerable extent Attempts to remove the offending substance may be effectual but efforts to push the bolus into the stomach with a tube may result in further penetration It is therefore mandatory to transfer the patient to an expert esophagoscopist meanwhile administering massive doses of sulfanilamide (p 88) or penicillin (p 106)

INJURY FROM INSTRUMENTATION

Injury to the esophagus caused by instrumentation particularly with *the esophagoscope is a matter of grave significance* In most instances the esophagoscope penetrates the mucous membrane producing a false passage to mediastinum pleura or lungs This injury may be accompanied by *shock* or may be silent until mediastinitis develops

Mediastinal injuries are often associated with a *subcutaneous emphysema* which follows the fascial planes of the neck (p 3509) producing sharply demarcated *cyanosis* and swelling with compression and obstruction of the *trachea* Urgent surgical intervention must be initiated if the patient s life is to be spared

Because of the danger of infection with penetrating and perforation wounds of the esophagus the prophylactic systemic use of penicillin (p 106) or sulfanilamide (p 88) is warranted

ing a clinical picture resembling *para esophageal* or *diaphragmatic herniation* (p 1803)

Symptoms caused by the short esophagus rarely appear until the patient reaches middle life There may be low *substernal pain* radiating to the left shoulder and arm resembling *angina pectoris* (p 890) or gastric symptoms identical with those of *peptic ulceration* (p 1780) In the latter instance *hematemesis* not infrequently occurs further obscuring the clinical picture

Diagnosis—The diagnosis of short esophagus is not possible without radiography or esophagoscopy

Treatment—*The treatment of symptoms arising from the short esophagus* is most unsatisfactory An abdominal girdle or corset may be fitted



Fig 388—Thoracic stomach with short esophagus *

to force upwards abdominal contents and diaphragm thus relieving pressure on the herniated portion of the stomach With ulceration in the sac the usual peptic ulcer regimen (p 1790) is employed but the outcome is rarely satisfactory

With persistence of symptoms and especially in the presence of hematemesis the surgeon *is consulted in the hope that it may be* possible to achieve a corrective procedure A *left phrenicectomy* has been attempted with the idea of elevating the left leaf of the diaphragm and relieving tension on the intrathoracic portion of the stomach *Intra-abdominal and transthoracic approaches* to the problem are fraught with danger but give some promise of success In consequence none of these radical surgical

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STRICTURES

Esophageal strictures usually result from burns secondary to the accidental ingestion of lye by children With increasing contraction of the scar the lumen may be so narrowed that nutrition cannot be maintained *Esophageal dilatation* (p 1723) by the experienced expert is a life saving measure

CHEMICAL BURNS

Chemical injury to the esophagus occurs when caustics or chemicals are swallowed accidentally or *with suicidal intent* *The most frequent accidental cause* is the swallowing of *lye* by children Burns from chemicals



Fig 390—Stenosis of the esophagus due to lye

taken with suicidal intent arise from the ingestion of bichloride of mercury sulfuric acid carbolic acid or iodine

Clinical Manifestations—So severe is the pain of the chemical burn that the patient is usually seen in severe shock or collapse

Treatment—The *immediate aims* of therapy include removal of the poison protection of the injured mucous membrane and supportive treatment for shock (p 928)

The attempt to remove the poison from the stomach by gastric tube increases the anguish of the sufferer and may add further mechanical injury to the already traumatized gullet Therefore the practitioner should ply the patient with a demulcent such as *milk* a dilute solution of *vin*

IRRADIATION BURNS

Irradiation treatment of thorax and mediastinum in which the esophagus receives inadvertent and excessive doses of ray may produce inflammatory disturbances in the gullet leading to ulceration and cicatrization *with stenosis*

TRACTION DIVERTICULA

Traction diverticula usually occur at the level of the bifurcation of the trachea or near the left main bronchus The causative mechanism is contraction of the scar of *tuberculous lymph nodes* (p *1136*) or distortions due to *scoliosis* (p *3059*)



Fig 389 —A traction diverticulum in the midesophagus of a woman forty four years of age with healed tuberculosis of the left apex and extensive pleural thickening at the base of the right lung The exposure was in the erect left anterior oblique position *

Traction diverticula are about 2 cm in diameter and are generally asymptomatic since their configuration is such as to enable ready emptying They may however be responsible for complications such as esophago bronchial fistula and mediastinal abscess Generally the condition is found incidentally during gastro intestinal fluoroscopy The radiologist should inform the patient as to the position in which emptying best occurs

Traction diverticula are contrasted to the *pulsion diverticula* (p *1730*) which generally occur *in the upper part of the pharyngo esophagus*

Treatment is not required unless other lesions such as esophagitis or cardiospasm are present Surgical intervention is contraindicated unless a grave *complication* is encountered

of a pulmonary or cardiac accident with shock chest pain and extreme dyspnea If the patient does not die immediately infections of the thoracic structures may develop

Diagnosis—Esophagoscopic examination definitively reveals the presence of esophageal peptic ulcer *A biopsy is required to give assurance* that the lesion is not malignant *Radiography* occasionally reveals an ulcer niche suggesting the diagnosis

Treatment—The treatment of peptic esophagitis or peptic ulcer of the esophagus is identical with that of ulcer of the stomach or duodenum (p 1790) *On very rare occasions the ulcer on healing produces a stricture* which requires *dilatation* (p 1723) if obstructive symptoms are to be avoided If stenosis of the esophagus is present *gastrostomy* (p 1759) may become necessary Gastrostomy has been used also for retrograde



Fig 391—Peptic ulcer of esophagus

dilatation These procedures are specialist province and require expert judgment

DECUBITUS ESOPHAGITIS

Decubitus esophagitis with or without ulcer is suspected when patients who are suffering from prolonged and severe illness complain of frequent regurgitation vomiting intractable substernal pain dysphagia and hematemesis The suspicion of an inflammatory esophageal lesion is *increased if it is known that previous treatment involved instrumentation* of the stomach and/or the intestines as in intestinal obstruction (p 1823)

When the esophageal decubitus complicates intubation it requires a nicety of judgment to decide whether to permit the mucous membrane to suffer continued irritation or whether the patient's best interest is served

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egar is given if lye has been swallowed and *bicarbonate of soda* is administered in the presence of acid ingestion

An attempt should be made to allay the pain by permitting the patient *to sip a 1 or 2 per cent cocaine solution* (p *3916*) or *10* per cent ethyl aminobenzoate (p 3916) Large doses of opiates (p 3853) or a basal anesthetic (p 3913) must be employed if the pain is to be successfully combated

The management of the immediate shock calls for the intravenous administration of fluids and salts By this means nutrition can be maintained so that a feeding *gastrostomy* (p 1759) should rarely be necessitated

Particularly with lye burns there is a tendency to the later formation of *stricture* In consequence, an esophagoscopist is consulted for dilatation of the gullet (p 1723) as a prophylactic procedure in the early phases and as a therapeutic procedure after the stricture has impaired general nutrition

PEPTIC ESOPHAGITIS AND PEPTIC ULCER OF THE ESOPHAGUS

Peptic esophagitis and ulceration relatively infrequent lesions of the gastro intestinal tract usually occur in persons between the ages of thirty and seventy years The origin and pathogenesis of peptic *ulcer of the* esophagus are probably similar to those of the gastroduodenal variety (p 1780) The location of the lesion may be dependent upon *heterotrophic islands of gastric mucous membrane* which persist in the lower portion of *the esophagus the acid reaction of this aberrant tissue* produces local erosion and ulceration An abnormally *patulous cardia* which permits regurgitation of acid gastric juice may be another factor which determines the site of the disturbance The location of the ulcer is generally in the lower 3 inches of the esophagus It is usually close to the cardia and occa*sionally extends into the stomach*

The histologic and pathologic characteristics are the same as those of ulcer of the stomach and duodenum Many ulcers heal without complications, occasionally a large ulcer in healing produces stenosis with proximal dilatation

Clinical Manifestations —Peptic ulcer of the esophagus may be asymptomatic until a major complication such as perforation or hemorrhage occurs The outstanding symptom otherwise is *pain* which is usually located about the xiphoid cartilage or retrosternally *Painful deglutition* may follow the eating of solid food but may be absent when liquids are taken *Dysphagia* occurring early in the course of the disease is probably due to spasm later it may be due to stenosis *Regurgitation* and *vomiting are frequently associated with peptic ulcer of the esophagus*

The complications are those of peptic ulcers elsewhere *Bleeding* is usually reflected as a hematemesis *perforation* occurs infrequently but is serious and frequently fatal since the communication may be *subdiaphragmatic* into the lesser peritoneal cavity or *supradiaphragmatic* into the contiguous structures of the mediastinum or the aorta The symptoms associated with the abdominal type of perforation are essentially those of a perforated gastric ulcer However the supradiaphragmatic perforation produces a totally different clinical picture which is much more suggestive

Treatment—*Direct visualization* of the gullet should reveal the presence of a malignant lesion that is sufficiently large to cause symptoms While the technical procedure of *esophagectomy* (p 1723) is formidable and associated with great risk conservative treatment offers only imminent death Inoperable lesions producing obstruction are treated by the



Fig 39 —Carcinoma of the esophagus

institution of a *feeding gastrostomy* or *jejunostomy* (p 1759) These palliative procedures not only prolong life but prevent indescribable suffering

Roentgen therapy and radium implantation for esophageal cancer have not yielded satisfactory results though irradiation may be used as an adjuvant to surgery

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by removal of the tube In the event of doubt the tube should be removed temporarily, to be replaced if the symptoms of intestinal obstruction again dominate the clinical picture

SECONDARY OR SYMPTOMATIC ESOPHAGITIS

A certain amount of esophagitis accompanies mechanical disturbances such as cardiospasm stricture diverticulitis or obstruction due to carcinoma Under these circumstances the esophagitis is of secondary importance and is relieved by therapy directed at the more fundamental condition

BENIGN NEOPLASMS OF THE ESOPHAGUS

Benign esophageal tumors (*papillomas lipomas* and *fibromas*) are of rare occurrence They have no clinical significance unless they become ulcerated or produce obstruction

CARCINOMA OF THE ESOPHAGUS

Carcinoma of the esophagus is most often found at one of the sites of physiologic narrowing in the postcricoidal region, contiguous to the left bronchus or near the hiatus It usually involves the lower third of the gullet The morphology is variable The *polypoid type* causes early obstruction an *ulcerating variety* produces anemia with early metastasis and the *scirrhous* cancer results in *stenosis* Distant *metastases* occur early and the *cervical lymph nodes* may be involved by direct extension

Clinical Manifestations —As with other malignant infiltrations the beginnings are insidious and consist of progressively increasing *dysphagia* which at first is present only when solid or dry foods are ingested As the lesion increases in size the patient is unable to swallow anything but liquids Even these are felt to stick substernally in the region of the lesion *Regurgitation* or *vomiting* may occur Occasionally lodgment of a *foreign body* in the esophagus may be the first symptom

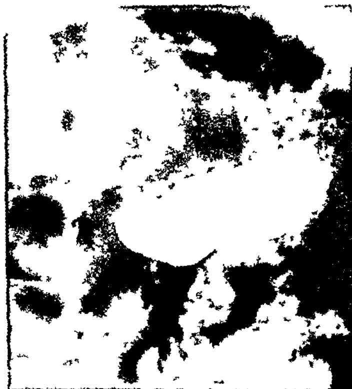
The esophagus above the level of obstruction due to carcinoma rarely dilates to a significant degree As a result the stalled esophageal contents flow over into the larynx, the patient complains of hacking *cough* which comes on after meals or upon reclining Later when the lesion has spread further to involve the recurrent laryngeal nerve regurgitation of food increases and is accompanied by *hoarseness* Hematemesis melena and secondary anemia may occur Metastases may be demonstrable in the supraclavicular or cervical lymph nodes On auscultation the swallowing sound may be absent

Diagnosis —The diagnosis of a malignant lesion of the esophagus should be considered when any patient beyond the age of thirty five complains of constant or increasing dysphagia *If the practitioner waits until the clinical diagnosis is obvious the chance for operative cure will have been missed* It is a far wiser practice to advise radiography and esophagoscopy even if a considerable number of patients are unnecessarily subjected to these unpleasant procedures *Biopsy* may be necessary to verify the nature of the lesion

Differentiation from cardiospasm is elsewhere discussed (p 1725)

Motor Funct on—The motor functions of the stomach are extremely complex In addi tion to the permutat ons and combinations which are possible with the three layered muscu lar wall of the stomach there is also a very active *muscularis mucosa* of great physiological and cl nical importance

Muscularis Mucosa—The mucous membrane of the stomach is freely movable over the muscularis *It is capable of independent movement and contraction due to the presence of* the muscularis mucosa which contains cir ular and longitudinal fibers As a result the *mucous membrane responds to stimulation with the most complex pattern of folds and de-* pressions On contact with a hard foreign body the muscularis mucosa is contracted in one area and relaxed in anoth r A *foreign body is so positioned that the mucous membrane is*



F g 893—Hypersthen c (steer horn) stomach with hypertonus increased rugal ma k n s and well filled duodenal cap

subjected to m n mal trauma It is this property of the muscularis mucosa which makes it so d fficult to interpret the ra l ograph c appearances frequently seen and often regarded as *g at rugae* Many of these mer ly r present contracted areas of the musc ilaris mucosa

Peristalsis—In add tion to contractions of the mus ularis mucosa ther exists a true per staltic contra tion n the stomach Peristaltic waves begin h gh up in the lesser curva tu e as small ripples whi h deepen as they ext nd downward when they reach the reg on of the incisura angularis they are almost always visible as d pressions of variable depth These waves us ially encircle the stomach and travel faster on the greater curvature than they do on the lesser curvature Not all of the waves extend to th pylorus most of them fade out a short d stance bel w the ne sura angularis F equently after two or three have passed a short d stance beyond the incisura the antrum contracts suddenly forcefully and violently As the antrum is the port n of the stomach contain ng the thickest muscle wall it is here

CHAPTER 88

THE STOMACH AND DUODENUM PHYSIOLOGY METHODS OF EXAMINATION AND TREATMENT

ANATOMIC REVIEW

See page 3560

THE PHYSIOLOGY OF THE STOMACH

In its role in digestion the stomach performs *secretory* and *motor functions* In addition the mucosa contains an *anti-anemic principle* essential to the development and maturation of erythrocytes (p 1038) The stomach chymifies some foods for further digestion in the succeeding tract and reduces most solids to semifluid consistency it absorbs little other than small quantities of water chloride and dextrose and ejects indigestible material and toxic substances excreted through its epithelium

Gastric Secretion—The gastric mucosa secretes *mucus pepsinogen* and *hydrochloric acid* in addition to a small amount of *lipolytic ferment* which is of no clinical importance

Mucus—Gastric mucus is secreted by *goblet cells* in response to mechanical or chemical irritation of the lining membrane Enclosed in this mucus are usually seen varying numbers of *leukocytes* as well as cast-off *debris* of the gastric mucosa Gastric mucin neutralizes varying amounts of hydrochloric acid and mechanically protects the mucosa from the eroding influence of acid It is of great importance in the prevention of ulceration and assists in healing

Pepsin—The chief or peptic cells secrete *pepsinogen* on contact with hydrochloric acid this pro-enzyme is converted into active pepsin which initiates the chain of digestive processes involving the protein constituents of food

Hydrochloric Acid—Hydrochloric acid is the product of *parietal* or *oxyntic cells* It is the only inorganic acid secreted in the body and is put forth at a concentration of about 160 millimoles or chemical units The titer of free hydrochloric acid in the stomach is usually reduced through neutralization by other components of gastric secretion and regurgitation of duodenal content through the pylorus

Hydrochloric acid has an efficient antiseptic action Its production is related to an adequate intake of the vitamin B complex

FACTORS CONTROLLING SECRETION—The *normal stomach* secretes 500 to 1000 cc of hydrochloric acid daily Hydrochloric acid is essential to peptic activity it converts pepsinogen to the active form of pepsin with pepsin it initiates the digestion of protein When acid enters the *duodenum* it acts as a secretory stimulant (*secretagogue*)

The secretion of hydrochloric acid is under a triple control There is a *psychic component* initiated by the smell taste sight thought or swallowing of food this *cephalic phase* is mediated through the *vagus nerve* and is eliminated by vagus denervation Secretion is also influenced by emotional states unrelated to food intake it is modified by anxiety fear fright, worry and resentment These latter factors are of greatest significance in the concept of the pathogenesis of *peptic ulcer* *Chemical control* is initiated through the antral mucosa On contact with food the antral mucosa liberates a hormone which travels in the blood to the parietal cells where it causes a secretion of hydrochloric acid The *intestinal phase* of secretion results from the contact of food with the mucosa of the small intestine especially the duodenum

In addition to the intestinal secretory mechanism there is an inhibitory hormone (*enterogastrone*) formed in the intestinal mucosa upon contact with fat *Enterogastrone* has the properties of depressing the secretion of hydrochloric acid and the motor function of the stomach This principle is utilized in the feeding of fats and olive oil in *ulcer therapy*

ACID AND HEMATOPOIESIS—Hydrochloric acid activates the *extrinsic factors* that are concerned with *hematopoiesis* In the treatment of anemia whether hypochromic or hyperchromic hydrochloric acid is included in the therapeutic regimen

THE PHYSIOLOGY OF THE DUODENUM

The duodenum like the stomach has motor and secretory functions

Ejection of Chyme —The ejection of the chyme into the duodenum produces a cone-shaped accumulation that gives the familiar fluoroscopic picture of the "cap" Peristaltic waves occur in the duodenum independent of gastric movement. Duodenal waves are rhythmic segmental movements with superimposed components which propel food onward into the intestines It is not at all uncommon to find *retroperistalsis* in the duodenum particularly with mechanical disturbances in the second and third portions

In the second portion of the duodenum the intestinal content is mixed with *bile* and *pancreatic secretion* The bolus usually moves rapidly through second and third portions but *there is often a delay* at the *duodenojejunal flexure* particularly if the angulation is unusually acute (*duodenal ileus*)

Secretory Function —The chemical function of the duodenum is concerned with the production *of secretin* The presence of *hydrochloric acid in the duodenum causes a local production* of this enzyme which enters the blood stream and stimulates pancreatic and biliary secretions

THE BACTERIOLOGY OF THE STOMACH AND DUODENUM

The bacterial flora of the stomach and duodenum is extremely varied The organisms of the mouth and throat are ingested and may be recovered from gastric or duodenal contents or both In addition the normal inhabitants of the intestinal tract may be carried by reverse peristalsis into the duodenum or even the stomach but the presence of large numbers of coliform bacteria in stomach or duodenum is definitely abnormal

The acidity of the stomach is usually sufficient to destroy most bacteria which should not be found in any great numbers Fungi yeasts and molds ingested with uncooked food may also be recovered *Tubercle bacilli* swallowed with sputum are often identified in gastric washings that have been concentrated and stained (p 51)

SPECIAL METHODS OF EXAMINING STOMACH AND DUODENUM

Examination of the stomach by routine methods of inspection and palpation reveals little *Tenderness* is often present in the epigastrium when inflammatory processes are operative By the time that a *mass* is palpable however a malignant gastric lesion is often inoperable and the diagnosis becomes of academic importance only

Late physical manifestations of gastric disorders include the *visible peristaltic wave* seen in the epigastrium in congenital pyloric stenosis of infancy (p 2735) and acquired stenoses of adult life The *Virchow node* of carcinomatous metastasis occasionally may be palpated in the left supraclavicular fossa The huge *epigastric protrusion* of a gastric dilatation points to the presence of a gastrectasis (p 1807)

Laboratory and Specialist Procedures —Because of the inaccessibility of the stomach to routine examination and the late appearance of subjective symptoms in malignancy special methods of examination are employed on slight suspicion It is better to perform hundreds of unnecessary gastric *examinations than to miss one which might save the life of a patient*

The special investigations which can be done by the practitioner in his office laboratory include *gastric and duodenal test meals* and *examinations of the stool* The radiologist contributes immeasurably to gastric examination by the performance of the gastro intestinal series using the barium meal and the *barium enema to delineate the lumen of the hollow* bowel Recently the armamentarium of the gastric examination has been augmented by the introduction of *gastroscopy* (p 1745) by which the interior of the stomach is visually subjected to scrutiny and *electrogastrography* which can be performed at little risk or discomfort

that most of the trituration of food is performed The secretory and motor functions of the stomach are synchronized

Ejection of Chyme —With antral contraction the pylorus opens The pressure within the stomach forces the food into the duodenum which relaxes to receive it In this fashion the stomach accomplishes the important function of ejecting food in small amounts into the small intestine

Gastric Sensitivity.—The gastric mucosa itself is insensitive to ordinary mechanical chemical or thermal stimuli Such sensations as arise from the stomach are the result of varying degrees of tension in its muscular walls and are conducted by way of the involuntary nervous system to the central nervous system



Fig 394 —Gastroptosis of fish hook variety with hypertonus increased rugal markings and well filled duodenal cap

As the stomach fills its muscle fibers slip over one another so that the internal gastric pressure increases very slightly if at all If the stomach is filled too rapidly there results an increase of intragastric pressure due to the failure of the muscle fibers to relax This mechanism is reflected as a sensation of *epigastric pressure* and *fullness*

Innervation of the Stomach—The stomach has a dual innervation through *cholinergic* and *adrenergic* fibers The cholinergic or vagus mechanism is motor and secretory *Vagal stimulation* produces acid secretion increased motor tone opening of the cardia and activation of peristalsis *Vagotomy* abolishes the cerebral phase of secretion decreases tone and lessens peristaltic activity Adrenergic effects are less clearly defined but probably decrease muscle tone and effect closure of the pylorus

have been completed with the small amounts Observations are repeated at 3 5 24 and 48 hour intervals If the stomach findings are suspicious at the fasting observation the meal can be repeated at the five hour period to observe whether defects are still demonstrable

Specialist Radiography—In the event of suspicious or positive findings the practitioner should refer the patient to the specialist roentgen

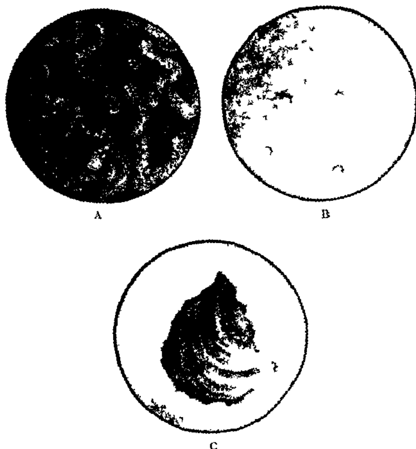


Fig 895—*A* Extreme hypertrophic gastritis The mucosal folds are very prominent and appear stiff and rigid The color of the mucosa is dark and highlights are absent Irregular small only slightly raised polygonal markings are present throughout *B* Hypertrophic gastritis with multiple superficial ulcerations The view shows the typical nodular character of the mucosa *C* A relatively normal gastrojejunostomy stoma (From original paintings by Ruth W Williams under the supervision of J F Monaghan from cases studied at the Graduate and Bryn Mawr Hospitals)

ologist Since the majority of gastro intestinal radiographs reveal no organic lesion the practitioner will rarely have to resort to consultation

Gastroscopy—By means of the gastroscope (p 1745) a flexible tube that can be introduced into the stomach the expert visualizes a major portion of the gastric mucous membrane In this way an early diagnosis

Gastric Test Meals—Gastric test meals (p 3721) reveal the secretory and motor processes The presence of *hypersecretion* and *hyperacidity* (p 1769) are not of great diagnostic significance but *anacidity* (p 1768) that is persistent after the injection of 0 5 to 1 mg (1⁄120 to 1⁄60 grain) of *histamine phosphate* (p 3723) strongly suggests the presence of a primary anemia or malignant lesion The latter suspicion is strengthened if the aspirated material is consistently stained with blood or blood pigment and the stool consistently gives a positive test for occult blood (p 3728) In primary anemia the blood findings are typical (p 1077) A *simple anacidity (p 1768) with acid secretion induced by histamine* is usually of little clinical importance provided there is no associated hematologic disorder

The *motor functions* are best tested by aspiration of fasting content after some recognizable substance (prunes or raisins) has been given the night before An excessive morning retention containing the skins furnishes incontrovertible evidence of an organic *pyloric obstruction* (p 1789)

Duodenal Contents—Examinations of duodenal contents (p 3726) are of importance in the study of disorders of liver biliary tract and pancreas They throw no light on alimentary disorders of the hollow viscera

The Stool—Gastric test meals are interpreted in the light of the examination of the stool A diet free from meat is given for three days On the fourth fifth and sixth days the stool specimen is collected and examined microscopically and chemically for the presence of blood (p 3728) and blood pigment In the absence of local bleeding from rectum or anus a persistently positive chemical test for blood indicates a gastro intestinal ulceration usually on a malignant basis The simultaneous presence of a histamine achylia strengthens that suspicion An associated hyperacidity suggests a large peptic ulcer

Occult blood may be detected in the stool much earlier than findings are demonstrable by radiographic examination In consequence the importance of this simple test cannot be overemphasized

Radiography—Radiography of the stomach and intestines after the barium meal is an obligatory procedure regardless of expense in the presence of any persistent or suspicious evidence of disturbances in the stomach or intestines These may be habitual gastric distress or pain persistent nausea or vomiting evidences of pyloric obstruction and gastric retention hyperacidity anacidity the persistent presence of occult blood in the stool or loss of weight without demonstrable explanation

The *practitioner radiologist* may readily learn the technic of gastro-intestinal radiography (p 3742) Fluoroscopy surpasses in importance and value the examination of dried roentgenograms Palpation during gastro-intestinal fluoroscopy serves to demonstrate lesions that cannot be depicted on films

Perhaps the most important single precaution in radiography of the stomach is the necessity of giving only small quantities of the mixture at the beginning of the examination The patient should swallow 1 to 2 ounces of the barium This quantity is forced by palpation to explore all surfaces of the stomach Larger quantities such as 10 to 16 ounces fill the stomach and obscure a small lesion particularly on the posterior surface The larger quantities of barium should not be ingested until examinations

Pancreatic	—	With acute hemorrhagic pancreatitis. Note rise of blood amylase. Fat necroses on laparotomy (p. 19..)
Splenic		In left upper quadrant, with splenic infarction particularly in subacute bacterial endocarditis. Get blood cultures (p. 54). With peri splenitis in any of the major splenomegalies. Examine hemogram and look for malarial and other parasites (p. 50)
Peritoneal		With acute and chronic peritonitis whether hematogenous, lymphogenous or of local origin. Consider abdominal puncture for identification of the invading organism (p. 1823). Pure cultures of pneumococci, gonococci or streptococci suggest generalized invasion amenable to nonoperative therapy. Mixed gram negative flora with fecal odor indicates localized lesion requiring laparotomy
Gynecologic		With acute salpingitis, oophoritis, pelvic peritonitis or rupture of ectopic pregnancy. Look for evidences of gravidity, gonorrhea or illegal abortion. Favor laparotomy when indications are equivocal. Institute supportive anti infective therapy under any circumstance
Lymphatic		With mesenteric lymphadenitis, particularly following upper respiratory infection or caseation due to tuberculosis. Favor laparotomy
Circulatory		With mesenteric thrombosis and passage of bloody stool. Consider laparotomy for resection of bowel

of *gastric ulcer* or of malignant lesion is possible. Contraindications to gastroscopy include the presence of any lesion which predisposes to perforation of the esophagus, gross deformity of the cervical or dorsal spine, aneurysm of the aorta, and corrosive and phlegmonous gastritis

Electrogastrography—The presence of *specific action currents* in the stomach have been demonstrated. Gastric curves obtained through an electrode introduced intranasally into the stomach may help to differentiate functional lesions, peptic ulcer and malignant lesions

DIFFERENTIAL DIAGNOSIS OF COMMON PRESENTING DIGESTIVE SYMPTOMS

The attention of the practitioner may be drawn to the digestive system by a variety of presenting symptoms and signs. The generic manifestations of involuntary rigidity of the abdominal wall, generalized abdominal pain and generalized abdominal swellings and tumors are presented in the tables which follow. Through them the reader is directed to more specific localizing symptoms in the various anatomic subdivisions of the abdomen

In addition the following references direct attention to other digestive complaints whose differential diagnostic problems are similarly tabulated and discussed

Anorexia (p 1779) *Polyphagia Bulimia and Pica* (p 1776) *Dyspepsia*

DIFFERENTIAL DIAGNOSIS OF

Involuntary Rigidity of the Abdominal Wall

Involuntary rigidity of the abdominal wall is always a finding of serious significance It demands meticulous examination and surgical consultation

Involuntary rigidity may be generalized or localized, it may arise as the result of a referred transmission from a distant organ or it may be due to inflammation of an underlying structure within the peritoneal cavity Rigidity is closely allied to the sensation of pain with which it is usually associated (p 1474)

	DIAGNOSTIC FEATURES
Extraperitoneal	
Circulatory	With coronary occlusion and pericarditis Get Ecg in all instances of acute indigestion
Respiratory	With lower lobe pleurisy and pneumonitis. Supplement chest examination with x ray (p 3740)
Urinary	Impaction of ureteral calculus Examine urine for red cells and crystals (p 3683) Obtain scout film for radiopaque shadows Refer to urologist for intravenous and retrograde urography and cystoscopy (p 2248)
Neurogenic	In gastric tabes with pupillary changes and positive serology in cerebrospinal fluid. In acute and chronic meningitis with characteristic findings in cerebrospinal fluid
Systemic Infection	With tetanus and history of penetrating wound. In epidemic pleurodynia pneumococcemia and meningococcemia Obtain blood culture (p 54)
Metabolic	In diabetic and other types of ketosis Examine urine for acetone and sugar (p 3680)
Toxic	In chronic alcoholism With lead poisoning Following snake and spider bites
Intraperitoneal	
Gastroduodenal	In acute gastritis particularly of alcoholic origin With penetration or perforation of peptic ulcer or gastric carcinoma Get gastric analysis and barium x ray (p 1744)
Intestinal	With acute appendicitis usually in right lower quadrant With penetration or perforation of ulcer neoplasm or diverticulum of small or large intestine With gangrene of thrombosed or obstructed intestinal loop Get x rays for demonstration of free air (p 1790) Consider abdominal puncture or laparotomy (p 1823)
Hepatic	In right upper quadrant, with localized peritonitis or abscess formation. Make therapeutic test with emetine if lesion is suspiciously amebic (p 525) Otherwise consider diagnostic puncture (p 1823) or laparotomy
Biliary	In right upper quadrant with cholecystitis and choledochitis and penetration, perforation or gangrene of gallbladder Seek radiopaque shadows (p 1938) Look for icterus (p 1951) Consider laparotomy

CONTINUED

Pharmacologic	Drastic catharsi Hyperperistalsis due to pit re sin, neostigmine and allied preparations Poisoning with mercury or lead. Overdosage of anthelmintics
Vegetative	Generalized spasmosis from emoti nal stre s or autonomic imbalance
Inflammatory	Nonspecific gastritis duodenitis il tis and colitis Regional ileitis and chronic nonspecific ulcerative colitis with evidences of psychoso matic abnormality (p 1651) Specif c inflam mations in typhoid and paratyphoid fever amebic and bacillary dysentery tuberculous enterocolitis and cholera Culture blood and stools for identification of pathogenic org nism (p 54) Examine serum for agglutinin titers (p 59)
Mechanical Disturbances	Acute dilatation of the stomach with copious returns following intubation Dynamic ileus from inte tinal obstruction with ab ence of flatus and feces and isolated dilatation of loops as seen by x ray Toxic ileus with generalized distention and pas age of feces and flatus
Uterine	Dysmenorrhea On t of labor Rupture of ectopic pregnancy Placenta prae ria
Inflammation of Peritoneal Surfaces (With Rigidity of the Abdominal Wall (p 1746)	Rupture of hollow abdominal viscus with demonstrable free air under diaphragms (p 1790) Hematogenous or lymphogenous peritonitis with streptococcus gonococcus pneumococcus or colon baci lus in pure cul ture of abdominal puncture (p 1823) Tuber culous peritonitis with positive findings after guinea pig inoculation (p 63) Localized peritonitis with diffu e spread after common lesion such as acute appendicitis acute cho lecystitis acute salpingitis or diverticulitis (p 1923) Acute hemorrhagic pancreatitis with elevation of blood amylase and areas of fat necrosis seen after laparotomy (p 1940)

(p 1770) *Hiccough* (p 1933) *Hematemesis* (p 1764) *Constipation* (p 1852) *Diarrhea* (p 1840) *Melena* (p 1843) *Jaundice* (p 1951) *Ascites* (p 1921) *Tympanites* (p 1878) *Incontinence of Feces* (p 1915) *Ano-perineal Pain* (p 1913) *Pruritus Ani* (p 1916) *Hepatomegaly* (p 1973) *Splenomegaly* (p 1131) *Disturbances of the Gastric Contents* (p 3721) *Disturbances of the Duodenal Contents* (p 3726) *Abnormalities Noted in the Stool* (p 3727)

SPECIAL METHODS OF TREATMENT OF STOMACH AND DUODENUM

In disorders of the stomach and duodenum special treatment methods include mechanical lavage the administration of topical medicaments and surgical procedures

Gastric Lavage and Intubation—Gastric lavage as previously practiced with the large Ewald tube no longer enjoys the popularity of former days At the present time it is used almost exclusively for the evacuation of

DIFFERENTIAL DIAGNOSIS OF

Generalized Abdominal Pain

The important problems relative to abdominal pain are considered in several localities The present concern is generalized abdominal distress Separate tables are provided for localized pains in right upper quadrant (p 1959) left upper quadrant (p 1942) epigastrium (p 178) hypogastrium (p 2302) left lower quadrant (p 1866) right lower quadrant (p 18o0) and umbilical region (p 1887)

In any instance the provocative mechanism for abdominal pain may be extraperitoneal or it may be a disturbance of the mucous membrane muscularis or peritoneal surface In the management of abdominal pain surgical consultation is mandatory for operative interference and for division of responsibility when a conservative policy seems the wiser course

	DIAGNOSTIC FEATURES
Extraperitoneal	
Infectious	Acute rheumatic fever with arthralgia rapid sedimentation time and favorable response to salicylates (p 186) Brucellosis with positive skin test (p 317) Trichinosis with eosinophilia and myalgias Typhoid fever with positive blood culture or rising agglutinin titer (p 59)
Respiratory	Lobar pneumonia acute pneumonitis and acute fibrinous pleurisy Supplement physical examination with x ray of chest
Circulatory	Angina pectoris coronary insufficiency or occlusion and acute pericarditis Note relief to angina with nitroglycerin (p 890) Observe friction rub in pericarditis (p 1007) Obtain Ecg in angina and coronary disturbances Mesenteric thromboses with blood in stools (p 994)
Hemic	Sickle cell anemia with characteristic hemogram (p 1065) Hemorrhagic capillary toxicosis with cutaneous purpura (p 1121) Hemolytic crises with icterus and increased fragility of red cells (p 1060)
Urinary	Impacted ureteral calculus Examine urine for red cells and crystals (p 3683) Get scout film for radiopaque shadows (p 2311) Refer to urologist for cystoscopy and urography
Metabolic	Hypoglycemia following overdosage with insulin Lead colic Snake and spider bite
Neurogenic	Gastric crisis of tabes with pupillary and spinal fluid changes (p 1464) Acute meningitis
Psychogenic	Hysteria
Pharmacologic	Withdrawal symptoms in drug habituation (p 3815)
Disturbances of Mucosa and Muscularis (Unaccompanied by Involuntary Rigidity)	
Errors in Hygiene	Dietary indiscretion, gluttony alcoholism, ingestion of irritant foods and abuse of spices Drinking ice water while over heated. Distention from carbonated drinks

CONTINUED

this tube It is best used with the cooperative patient who has learned the knack of swallowing the bucket The great advantage of the Rehfuss type of tube is the fact that the patient swallows the bucket hence it is virtually impossible for any respiratory accident to occur

The third type of stomach tube is exemplified by the *Levine model* in which the tubing is of the same caliber as the Rehfuss model but stiffer At the gastric end instead of the metal bucket there are several openings as in a catheter The Levine tube is passed through the nostril or the mouth It can be employed for every type of gastric or duodenal procedure

Technic of Introduction—*Bridge work* and *removable dentures* are taken out before any type of gastric tube is passed If it is possible the patient should sit upright during the passage of the stomach tube He is instructed to breathe forcibly during the passage of the tube to depress the chin on the chest so that the swallowing is facilitated and to avoid coughing gagging holding the breath raising the chin or manually removing the tube or interfering with the hand of the medical attendant

Gastric tubes should be *iced* and *lubricated* with a greaseless substance The Ewald and Levine types are actively passed into the stomach Particularly in children and patients who are unconscious or stuporous the greatest care must be observed lest the tube inadvertently enter the respiratory passages Should this occur the patient will usually cough and the examiner detects expiration through the tubal orifice The exhaled air may be felt against the examiner s cheek or a film of soap placed over the orifice will give visible evidence of expiration by the appearance of bubbles

Nothing is to be passed into the tube until aspiration demonstrates the presence of gastric contents

The distance from the incisor teeth to the cardia averages 40 cm Most of the tubes are clearly marked at the various distances Aspiration of stomach content is best accomplished when the tube has been passed approximately 55 cm though there are many individual variants most particularly in the patient with gastroptosis

Aspiration of the Gastric Contents—No matter what treatment is planned the gastric contents should be aspirated to verify the presence of the tube in the stomach Using the Ewald tube aspiration is performed by a large rubber bulb For the smaller types of tube it is much more satisfactory to use a glass syringe so that the amount and character of the fluid may be observed This is of particular significance in the presence of bleeding

Aspiration is frequently interrupted when gross particles plug the lumen of the tubing or when the mucosa adheres to the orifices Under such circumstances the syringe is temporarily disconnected A few cubic centimeters of the air are forcibly introduced to dislodge the foreign body or the mucous membrane

Gastric Lavage—As soon as the stomach is empty lavage is started The patient may drink the lavage fluid along the side of the tubing The fluid may be introduced through the tubing by means of a syringe

Warm tap water is perfectly adequate for gastric lavage If there is a suspicion of alkaloidal poisoning warm tea is the most convenient vehicle containing an alkaloidal precipitant (tannic acid) If the gastric contents

the stomach in the presence of an organic stenosis (p 1789) or a suspected poisoning (p 743) The vogue for repeated gastric washings in the treatment of peptic ulcer and inflammatory disturbances of the stomach has fortunately fallen into disuse

Gastric intubation using the Rehfuss Levine or Miller Abbott tube is of tremendous value in the prevention and treatment of acute gastric dilatation (p 1807) and intestinal ileus (p 1857) Occasionally the tube is introduced for the continuous milk drip in ulcer therapy (p 1759)

DIFFERENTIAL DIAGNOSIS OF

Generalized Abdominal Swellings Due to Solid Tumors

Except for the enlargement of the uterus as seen in the last months of pregnancy solid abdominal tumors are infrequently encountered The practitioner is more often confronted with diagnostic problems referable to tympanites (p 1878) or ascites (p 1921) or with the identification of localized tumors in the epigastrium (p 1814) right upper quadrant (p 1957) left upper quadrant (p 1849) right lower quadrant (p 1880) left lower quadrant (p 1870) or hypogastrium

	DIAGNOSTIC FEATURES
Pregnancy	Particularly with multiple births and hydramnios Confirm pelvic finding with urinary tests for gravidity (p 2496)
Gastric	Dilatation of stomach due to toxemia or obstruction Evacuate by stomach tube (p 1749) Examine gastric content for acidity and occult blood (p 3721) Myosarcoma recognized at laparotomy
Colonic	In Hirschsprung s disease (congenital megacolon) Confirm by barium enema
Cystic	Ovarian omental or pancreatic Avoid abdominal puncture and confirm by laparotomy
Helminthes	Hydatid or echinococcus disease Note eosinophilia Attempt to elicit thrill over tumor mass Establish immunologic diagnosis by complement fixation or intracutaneous reaction (p 50) Prepare for laparotomy
Vascular	Aneurysm of abdominal aorta with diffuse pulsation

Types of Stomach Tube —Three types of stomach tube are in common usage The *Ewald* or *Boas* tube is constructed of reasonably stiff rubber It measures about 14 mm in diameter, and is usually passed by the physician into the patient s stomach Some patients learn to pass the tube themselves The Ewald tube can be tolerated only for a very few moments and its use is limited to gastric lavage in the cooperative patient

The *Rehfuss* model is of soft rubber tubing about 4 mm in diameter at the gastric end of which there is a metal bucket The bucket and tube may remain in the stomach for an indefinite time Lavage gavage duodenal drainage and transduodenal lavage are successfully executed with

rived from the common duct and gallbladder Later a thin golden yellow bile makes its appearance

This type of biliary drainage is described as *nonsurgical* drainage of the biliary tract

Withdrawal of the Tube—Whatever type of tube is employed the end is pinched off during withdrawal The tube is removed with the greatest rapidity In the Rehfuss type of tube with the metal bucket at the end the teeth are protected by the introduction of the examiner s fingers into the mouth so that the metal tube hits the fingers placed against the lingual surfaces of the teeth

If the tube is to be kept in place for any length of time the nose and throat are sprayed and lubricated with albolene A decubitus or pressure ulcer of the esophagus may be caused by the tube particularly in patients who are comatose

Gastric Medication by Topical or Local Application

The prevalence of gastric symptomatology is attested by the wide use of proprietary preparations aimed at the alleviation of upper abdominal distress Fortune Magazine * in a survey (1941) estimated that the Great American Stomach is particularly susceptible to self treatment and is a supporting pillar of the drug trade both ethical and proprietary 'Most large druggists stock nearly 200 preparations designed to dispel nausea relieve gas loosen the bowels sooth inflamed mucosa and otherwise alle viate distress in the gastro intestinal tract All told there are probably 500 separate branded powders pills and potions manufactured for the Great American Stomach and environs in addition to the tons of sodium bicarbonate and other common alkalies universally employed plus huge numbers of hot water bottles enema bags and similar mechanical appara tuses and contraptions

Gastric medicaments include acids ferments antacids pepsin inactiva tor protectives stimulants irritants and rubefacients absorbents emetics antemetics sedatives and local anesthetics

Acids—*Dilute Hydrochloric Acid* (*U.S.P*) is of 10 per cent strength The usual dose is 2 cc or 30 drops added to a half glass of water and sipped through a drinking tube to prevent ill effects on the teeth This official dosage is undoubtedly too small The patient should be urged to increase the dose to tolerance The single dose may be increased to 4 cc To obtain an effectual amount the patient takes a dose one hour before meals sips another with the meal and if possible a third dose after the meal In this way nine doses may be ingested daily approximating a total of 18 to 36 cc Once the use of hydrochloric acid has been initiated it is to be continued indefinitely If the medication is stopped the patient should be instructed to resume its use upon the reappearance of symptoms

In addition to the official hydrochloric acid a commercial preparation of the *hydrochlorides of glutamic acid* is available in convenient capsule and tablet form It provides less free acid at greater expense

In the *primary anemias* (p 1077) in which anacidity is invariably pres ent the use of hydrochloric acid is mandatory In the *secondary anemias*

* From The Gr at Ame ican Stomach Fortune December 1941 p 83

show thick tenacious mucus the lavage may be carried out with a solution of bicarbonate of soda, employing a teaspoonful to a pint of water

The lavage is continued until the washings are quite clear It is interrupted instantly when there is any appreciable amount of blood If there is a suspicion of poisoning the lavage fluid is preserved for examination by the authorities

Gastric Gavage and Milk Drip —Gavage or tube feeding is performed under circumstances where the patient cannot or will not accept nourishment The gavage fluids include citrated milk, fruit juice egg nog or aqueous solutions containing sugar and/or salt

For gastric gavage the fluid metabolic and vitamin requirements may be met by the use of the following mixture which yields 2700 calories in a volume of 1600 cc

6 eggs thoroughly beaten
½ pint of cream
½ pint of tomato juice
1½ pints of milk
1¼ cups of corn syrup
1 teaspoonful of salt
1 cc of viosterol
1 tablespoonful Brewer s yeast

A modification of gastric gavage suggested in the treatment of patients who suffer from nocturnal hyperacidity, is the *milk drip*

For the milk drip the patient is permitted to fall asleep with the Rehfuss or Levine tube in the stomach The free end of the tube is connected to a reservoir containing citrated milk with or without an antacid or a colloidal demulcent The rate of flow is controlled as in the intravenous drip by a Hoffman clamp The number of drops may be counted in a Murphy drip interpolated in the rubber tubing beneath the clamp

Continuous Gastric Drainage —In the various types of gastric or intestinal obstruction whether mechanical or paralytic, the stomach may be drained continuously by means of the indwelling Levine or Rehfuss tube The tube is introduced the gastric contents aspirated and the stomach washed The free end of the tube is then allowed to drain into a vessel or it is attached to a suction device

Continuous stomach drainage is accompanied by loss of water and chloride It is essential that a continuous intravenous drip of saline solution be employed for the patient who is having continuous gastric lavage

Duodenal Drainage and Lavage —Duodenal drainage and lavage are carried out by the same technic as gastric drainage and lavage The Rehfuss type of tube is employed It is passed to the 75 cm mark—the patient lying on the right side for at least twenty minutes Recovery of clear bile on aspiration is definitive evidence that the tip of the tube has entered the duodenum

Biliary drainage is stimulated by the intraduodenal instillation of 50 cc of a 33 per cent solution of magnesium sulfate or of 33 cc of olive oil Five minutes after the introduction of the saline or oily solution the fluid is aspirated Thereafter the bile is permitted to drip from the end of the tube into a receptacle The first specimens of thick bile are believed to be de-

is *Sodium Bicarbonate U.S.P* When soda is administered it reacts with hydrochloric acid liberating carbon dioxide The patient experiences rapid relief from symptoms due to the presence of excess acid The duration of the action is short The drug rapidly leaves the stomach and is reabsorbed in the intestinal tract Excess of bicarbonate enters the blood and tends to produce a *systemic alkalosis*

The absorbable antacids have many disadvantages They inhibit protein digestion by creating a neutral or alkaline medium the alkaline phase is frequently followed by a stimulation of acid secretion so that the titer after the administration of an alkali is higher than at the pre treatment level

THE NON ABSORBABLE ANTACIDS —The nonabsorbable antacids are slower in action than the systemic type and their effect is of longer duration they do not cause the liberation of carbon dioxide nor do they produce systemic effects such as alkalosis and tetany An additional advantage of the nonabsorbable antacids is the fact that they often act as gentle laxatives when they are excreted into the intestines

1 MAGNESIUM SALTS —The most frequently used nonabsorbable antacids are the salts of magnesium and calcium The official antacid *magnesium salts* include *Magnesium Oxide (light magnesia) U.S.P* and *Heavy Magnesium Oxide (heavy magnesia) U.S.P Magnesium Carbonate U.S.P* is used interchangeably with the oxide One of the most popular of the magnesium salts is *Magnesia Magma (Milk of Magnesia) U.S.P* containing approximately 8 per cent of the drug *Magnesium Trisilicate* is an insoluble tasteless, white powder that functions powerfully as a nonsystemic antacid and absorbent The usual dose varies from 1 to 4 gm

2 CALCIUM SALTS —The basic salts of calcium produce the same nonsystemic effects as those of magnesium Unlike the magnesium salts they tend to precipitate in the intestinal tract and are apt to produce *constipation* rather than a gentle laxative action Any excess may also produce calcium concretions in the urinary passages

The official calcium preparations are the *Precipitated Calcium Carbonate U.S.P* and *Precipitated Chalk U.S.P* Calcium hydroxide is often prescribed as the official *Solution of Calcium Hydroxide (Lime Water) U.S.P* This substance is so feebly antacid that it is impractical for clinical use

The *antacid powders* used in conjunction with the *Sippy diet* (p 1791) for the control of gastric ulcer consist of

1 ℞	Magnesium Oxide (heavy)	0 7 gm (10 grains)
	Sodium Bicarbonate	0 7 gm (10 grains)
2 ℞	Calcium Carbonate	0 7 gm. (10 grains)
	Sodium Bicarbonate	2 0 gm (30 grains)

These powders are alternated or administered in varying proportions depending upon whether there is an associated constipation or diarrhea The dose should be adjusted so as to achieve normal bowel movement as well as the neutralization of the gastric acids

Amphoteric Substances —Amphoteric substances neutralize hydrochloric acid The most popularly employed product is *Aluminum Hydroxide U.S.P* usually prescribed in the colloidal form as a solid or a liquid (Amphojel)

(p 1089), the acid factor may function synergistically as a hematinic with the iron

It is estimated that *subacidity* and *anacidity* occur in about 10 per cent of the population Although few patients with low acid figures suffer as the result of the physiological disturbance nevertheless the administration of hydrochloric acid has wide therapeutic utility The prescription for hydrochloric acid is considered in *diarrheas* of unknown origin (p 1840) in patients with *anorexia* (p 1779) or distaste for food and for those who are *underweight* and *asthenic* (p 2890) It is not necessary to analyze the gastric contents before prescribing hydrochloric acid The therapeutic test is simpler and more satisfactory

Gastric Ferments—The proteolytic enzyme *pepsin* is official in the *U S P* *It is so prepared that one part will digest 3000 times its own weight* of egg albumin It furnishes an excellent example of a preparation that is pharmacologically active and therapeutically useless This paradox is readily understood when it is realized that the normal stomach secretes an abundance of pepsin so that there is no need for a supplementary supply Gastric pepsin becomes insufficient only when the destruction of the stomach is so advanced that therapy is futile When the stomach has been surgically removed *as in subtotal gastrectomy the digestion of the protein* is accomplished satisfactorily by the pancreatic and intestinal ferments

The official *Elixir of Pepsin* (*N.F*) is used as a vehicle because of its pleasant taste

Antacids—Gastric antacids are so commonly employed by the laity that they are sold as confections Antacids are administered in powder form as compressed tablets and as candies flavored with sugar and a volatile oil usually peppermint

The widespread use of the gastric antacids is due to the conception that most instances of indigestion result from increased acid secretion by the stomach There is much reason to doubt the validity of this hypothesis Gastric analyses often reveal high acid figures when there are no symptoms and hyperacidity symptoms may be present in individuals who have normal or even low acid figures in the gastric analyses

There are many authorities who believe that the gastric symptoms of hyperacidity are more likely related to the motor activities of the stomach Hence the indication is for the administration of an *antispasmodic* (p 3892) or a *protective* (p 1756) The symptoms designated hyperacidity *more likely than not are a response to a local or* distant disturbance often psychogenic Under these circumstances treatment with an antacid relieves the subjective symptoms but clouds the fundamental etiological disturbance

Gastric antacids are chemical or physical in their actions *Chemical antacids* produce their effects by neutralizing the hydrochloric acid of the gastric contents *physical antacids* bind the hydrochloric acid by absorption the acid radicals remaining unchanged

Chemical Antacids—The chemical antacids are absorbable or nonabsorbable *Absorbable* antacid may cause a disturbance of the acid base balance of the blood *nonabsorbable* antacids do not tend to produce systemic alkalosis (p 722)

THE ABSORBABLE ANTACIDS—The most widely used absorbable antacid

preparations commonly employed are *peppermint anise* or *clove* Most ant acid preparations gastric sedatives and bitters contain the volatile oils for flavoring and as an accessory therapeutic measure

The administration of the volatile oil has a motor effect on the stomach The gas bubble that is trapped in the fundus of the stomach is usually disgorged with an audible and often highly satisfactory belch Contrary to common belief the formation of this gas bubble is not the result of fermentation in the stomach but of *air swallowing* (*aerophagia*)

Alcohol—The most important of app tizers and stomachics is alcohol (U S P) which functions as a gastric rubefacient and irritant Commonly it is prescribed with the bitters volatile oil or both The pleasantest prescription is the *before dinner cocktail* which is usually concocted with an alcoholic beverage a volatile oil and a dash of bitters The *postprandial* use of alcohol is essentially carminative irritation and rubefaction of the stomach tend to increase motility and speed gastric emptying In its pleasantest form alcohol may be employed for this purpose as a sweetened liqueur such as creme de menthe or the brandies of various types

Gastric Ferments—Many appetizers contain gastric ferments Any useful effect results from the employment of the vehicle rather than the enzyme

Adsorbents—A frequent gastric complaint is flatulence and a sense of fullness in the epigastrium This is usually due to the presence of a large air bubble in the fundus resulting from the swallowing of air or to increased intragastric tension The laity uses gastric adsorbents in large quantities The most commonly employed of these substances is *charcoal* in tablet form or in the insoluble shake mixture

A most useful prescription is the Mistura Nigra

℞		
	Sodium Phenobarbital	0 5
	Charcoal	6 0
	Peppermint Oil	1 0
	Pepsin	1 0
	Glycerin	20 0
	Water	120 0
	Sig One teaspoonful after meals	
	Shake well label	

Emetics—Emesis may be obtained by central stimulation of the vomiting area in the medulla This effect is produced particularly by *apomorphine* (p 3854) The most commonly employed emetics for local use are *mustard* and *ipecac* These are given in doses of 1 teaspoonful (4 cc) every ten or fifteen minutes until vomiting occurs The commercial brand of mustard is usually employed ipecac is administered as the official syrup Beside their usefulness in evacuating the stomach the emetics are also *vagal stimulants* and may be utilized to terminate attacks of paroxysmal cardiac irregularity (p 873)

The more toxic emetics include *tartar* which is mentioned only to be condemned since its absorption may give rise to serious distant symptoms

It may not be amiss to remind the practitioner that the stomach may most safely be emptied by mechanical means Emesis is often produced by irritating the pharynx with a tongue blade or the finger and lavage is best executed through the stomach tube (p 1749)

The physical absorbents do not produce local or systemic alkaline change The colloidal compounds are effective *demulcents* and *protectives* as well as antacids The single disadvantage to their use is the fact that they may form large gelatinous masses of sufficient bulk to produce intestinal obstruction (p 1873)

Summary—The therapeutics of antacids may be summarized by stating a preference for the *nonabsorbable magnesium salts* and the amphoteric preparations of *aluminum*

Pepsin Inactivators—A promising innovation in gastric therapeutics is sodium alkyl sulfate used in 0 2 gm doses every two hours as a pepsin inactivator

Gastric Protectives—The gastric mucous membrane is protected by barium bismuth and cerium salts gastric mucin and charcoal

Barium Bismuth and Cerium Salts—The salts of barium bismuth and cerium are used as protectives for the gastric mucous membrane Those most commonly employed are *Cerium Oxalate U.S.P* and *Bismuth Subcarbonate U.S.P* These are usually combined in equal parts in doses of 0 6 to 2 gm (10 to 30 grains) with the addition of a volatile oil such as Oil of Peppermint and a flavoring agent They are rarely absorbed in sufficient amount to cause toxic symptoms

A liquid prescription is as follows

℞	Cerium Oxalate	10.0
	Bismuth Subcarbonate	10 0
	Cinnamon Water q.s a d	60 0
	Sig One teaspoonful as directed	
	Shake well label	

Gastric Mucin—Gastric mucin N N R provides physical protection to the mucous membrane of the stomach and also functions as an antacid It combines with hydrochloric acid in the proportion of 1 gm to 15 cc of tenth normal hydrochloric acid Gastric mucin does not produce local or systemic chemical changes *The taste is unpleasant and cannot be effectively disguised* The dose is a teaspoonful in a full glass of water

Mistura Nigra—Since gastric distress is usually psychogenic the most effective gastric sedation is provided by preparations such as Mistura Nigra (p 1757) which contains charcoal and phenobarbital

Stimulants Irritants and Rubefacients—Mild irritants and rubefacients employed to further gastric digestion are the carminatives stomachics bitters and tonics

Bitters and Tonics—The bitters owe their efficacy to irritation of the gastric mucosa which causes the gastric secretions to be poured forth in unusual amounts The most commonly employed *bitters* include Compound Tincture of Gentian U.S P Tincture of Nux Vomica U.S.P and the Tinctures of Cardamom Calumba or Condurango The principle of employing bitters is recognized in the preparation of cocktails most of which are made with at least a dash of bitters The dose of the *tinctures* is 4 cc with the exception of Nux Vomica which should be prescribed in *amounts no greater* than 0 8 cc

Volatile Oils—Volatile oils stimulate the appetite In association with the bitters they evoke gastric secretion through a rubefacient effect The

preparations commonly employed are *peppermint* *anise* or *clove* Most ant acid preparations gastric sedatives and bitters contain the volatile oils for flavoring and as an accessory therapeutic measure

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Antiemetics, Sedatives and Local Anesthetics—Antacids such as bicarbonate of soda, *protectives* such as cerium oxalate and bismuth subcarbonate and *gastric mucin* are employed to allay nausea and vomiting Much more important in the symptomatic treatment of vomiting is the removal of the etiologic agent or the emptying of the gastric content by stomach tube

When vomiting is intractable *benzocaine* (3 to 10 per cent) *chlorbutanol* (1 to 2 per cent) or *cocaine hydrochloride* (1 to 2 per cent) may be administered to anesthetize the irritated gastric mucosa At times a *carbonated carminative* is extremely useful, this is obtained as *ginger ale* or the alcoholic carbonated drinks such as *champagne* The latter substance is tolerated when no other fluid or food is kept in the stomach

Gastric sedation may be accomplished by means of a *poultice* such as mashed potato or a thick cereal gruel which is too thick to vomit

Operations on the Stomach and Duodenum

Many operative procedures are utilized for the relief of organic abnormalities of the stomach and duodenum They range from simple suture (gastrorrhaphy) to almost complete removal (total gastrectomy)

Special Preoperative Measures in Gastroduodenal Surgery—Preparatory to operation the gastric patient is fortified by local and systemic treatment An attempt is made to effect healing of an ulcer by a conservative medical regimen (p 1790) If there is dilatation of the stomach tonus is restored by gastric lavage and if necessary the use of an indwelling gastric tube (p 1749)

Systemic therapy aims to correct the anemia that results from prolonged or brisk bleeding and to restore a normal electrolyte pattern (p 5) Patients who have had persistent vomiting are apt to be dehydrated and may be in severe alkalosis The latter state is often increased by the large amounts of antacids so commonly employed

Before any major gastric resection is attempted the patient s blood is grouped in case transfusion becomes necessary An intravenous drip is instituted to correct dehydration combat shock and combat fluid loss during operation The procedure facilitates emergency transfusion if the latter becomes indicated

Gastrorraphy and Duodenorrhaphy—Gastrorraphy or duodenorrhaphy is performed in cases of traumatic rupture or perforation of stomach or duodenum The operative risk varies with the duration of the perforation and the degree of resultant peritonitis In early perforations the risk is relatively slight When the perforation is of long duration the risk increases proportionately The prognosis in perforations of more than 12 hours duration is almost uniformly bad although the systemic and local use of sulfonamides (p 88) and/or penicillin gives promise of a reduction in mortality

Gastrotomy and Gastrorrhaphy—Gastrotomy consists of incision into the stomach and closure by suture It is performed for purposes of *exploration* of the interior of the stomach in instances in which the nature of an intragastric abnormality cannot be determined by nonoperative diagnostic methods and for the *removal of foreign bodies* (p 1807) which are too large

or of such shape as to be unable to pass the pylorus spontaneously This procedure ordinarily is associated with only slight risk Closure of the stomach constitutes the gastrorrhaphy

Gastrostomy and Jejunostomy—Gastrostomy creates an external opening into the stomach for purposes of direct feeding The opening usually is maintained by a tube which passes through the anterior abdominal wall in the left upper quadrant While the operation itself is simple the risk is greater than would be expected for the reason that the patient usually is in poor condition as the result of prolonged starvation and cachexia *Jejunostomy* is a similar opening into the small bowel and is utilized when the obstruction is in the stomach

Pyloroplasty—Pyloroplasty is performed for the relief of obstructions of the pylorus These most commonly are due to cicatrization of healed ulcers (p 1789) congenital atresias and hypertrophic pyloric stenosis (p 1797)

Pyloroplasty is performed by a number of methods Some of these (Rammstedt) involve merely the division of the serous and muscular coats of the pylorus without opening the lumen of the pyloric canal Other procedures require incisions of varying size through the pyloric wall and juxta pyloric portions of stomach and duodenum In the latter the opening is sutured so as to enlarge the lumen of the pyloric canal The risk varies from approximately 2 to 10 per cent depending upon the nature and extent of the procedure and the patient risk (p 3997)

Partial Gastrectomy and Gastrorrhaphy—Local excision is performed in cases of benign tumor or cysts of the gastric wall Occasionally peptic ulcer is treated by local excision combined with gastrojejunostomy Local excision is attended with relatively little risk

Gastrojejunostomy or Gastro enterostomy—Gastrojejunostomy or gastro enterostomy is performed in obstruction of the distal portion of the stomach pylorus or duodenum and in peptic ulcer unassociated with obstruction

When the anastomosis is performed for an obstruction due to the ulcer *in the distal portion of the stomach pylorus or duodenum* the operation is attended by a varying risk depending upon the experience of the surgeon The range of operative mortality is 0.5 to 5 0 per cent In obstructions due to carcinoma of the stomach the procedure is merely palliative and the risk rises to 3 to 30 per cent again depending upon the skill of the surgeon and the patient risk (p 3997)

With nonobstructed peptic ulcer (p 1780) the operation shunts gastric contents past the area of ulceration in order to diminish local irritation Regurgitation of alkaline intestinal contents also tends to neutralize excessive gastric acidity Unfortunately the procedure is usually unsuccessful If there is no obstruction the stoma closes spontaneously Should the stoma remain open for any length of time a marginal ulcer similar to the peptic variety is apt to occur at the site of the anastomosis

Gastric Resection (Complete Partial or Subtotal Gastrectomy)—*Complete gastric resection* is occasionally performed for extensive malignant disease of the stomach After removal of the stomach the esophagus is anastomosed to the upper portion of the jejunum just beyond the duodenum The risk is great the mortality exceeding 30 per cent in the most expert

hands The operation is often combined with splenectomy and removal of the omentum

Partial or subtotal gastrectomy is performed for less extensive malignant tumors for gastric ulcer and by some surgeons for duodenal ulcer The procedure requires exacting technic and is the province of the specialist in abdominal surgery The four major vessels of the stomach are ligated at the site of excision before the stomach is amputated Subtotal gastrectomy consists of the excision of two thirds to four fifths of the stomach beginning just distal to the pylorus and extending upward in such fashion that most of the greater curvature is excised The duodenal stump is closed by several layers of sutures the line of incision in stomach is sutured and a loop of jejunum is anastomosed to stomach by utilizing part of the original incision in the stomach or through a new incision the jejunal loop is brought up through the rent in the transverse mesocolon (*posterior or retrocolic anastomosis*) or it may be brought up in front of the colon (*anterior or antecolic anastomosis*) Occasionally an additional entero-enterostomy is made between afferent and efferent loops of jejunum Simultaneous bilateral vagotomy reduces motor and secretory activities

The *mortality* of a subtotal gastrectomy varies considerably with the experience of the surgeon In patients with carcinoma the immediate mortality varies between 10 and 50 per cent, in ulcer the mortality ranges between 2 and 20 per cent, depending upon the condition of the patient and the skill of the surgeon Despite the formidability of subtotal gastrectomy the operation has very little more risk than gastro enterostomy and the results are far better It attempts radical cure of cancer of the stomach and removes ulcer bearing and acid stimulating membranes of stomach and duodenum in peptic ulcer

Vagotomy —Bilateral supra or infra diaphragmatic vagotomy of itself may control motor and secretory activity precluding the necessity for more formidable procedures

Special Postoperative Measures in Gastro duodenal Surgery —After major gastric operations it is preferable to leave a stomach tube in place to prevent gastric dilatation The tube drains for about forty eight hours after which it is clamped off periodically for two hour intervals and fluids are administered by mouth in small quantities At the end of each two-hour interval the tube is unclamped and aspirated If the amount of fluid aspirated exceeds the amount which has been given by mouth it may be presumed that there has been regurgitation from the upper intestinal tract into the stomach Under such circumstances the tube is left in place and the procedure is repeated until aspiration reveals that less fluid is drained from the stomach than was taken by mouth At this time the stomach tube may be removed and the patient is given fluid by mouth in increasing quantities While the stomach tube is in place the intravenous drip is continued so that the patient is supplied with fluid salt amino acid vitamin plasma and/or blood As soon as the digestive functions are resumed satisfactorily the drip is discontinued

During the first twelve to twenty four hours drainage from the stomach tube may be discolored by dark blood If active bleeding persists and cannot be controlled by gentle lavage with warm water it may be necessary to re explore and ligate the responsible vessel

Postoperative Complications—Postoperative *pulmonary complications* are quite frequent following operation on the stomach (p 4017) and there is considerable risk of *intraperitoneal suppurative complications* resulting from leaks at one of the suture lines Treatment is that of peritonitis (p 1935) using sedation anti infective agents and continuous gastric aspiration The peritonitis may subside or leave localized purulent collections in the subdiaphragmatic space subhepatic space or pelvis these require appropriate incision and drainage

Occasionally *leaks of the suture line* result in spillage of duodenal or gastric fluid through the wound The extravasated fluid may digest the surrounding skin unless it is protected by an ointment meanwhile the intragastric fluids are removed by suction

Intestinal obstruction may complicate the postoperative course it may be due to angulation of the bowel at the site of the anastomosis or at the point of passage through meso colon *Treatment* should be conservative at first for with subsidence of postoperative edema the obstruction may spontaneously subside

Postoperative Gastric Diets—See pp 684–687

CHAPTER 89

CLINICAL DISTURBANCES OF THE STOMACH AND DUODENUM LOCAL MANIFESTATIONS OF SYSTEMIC DISORDERS

The stomach and duodenum sensitively reflect local manifestations of more fundamental and widespread disturbance Local lesions are also encountered which may or may not have secondary systemic consequences

The division between local lesions and local manifestations of systemic disorders which is tabulated on p 1763 has more than academic significance Particularly in gastric neuroses and peptic ulcer the broader viewpoint may determine success or failure of treatment the more useful routines recognize the importance of treating the individual rather than his gastroduodenal mucous membrane

VASCULAR DISTURBANCES

CHRONIC PASSIVE CONGESTION

Chronic passive congestion of the stomach is part of the general picture of *backward failure* (p 941) Its clinical importance arises from the fact that local engorgement may produce *anorexia* and *vomiting* Under these circumstances the clinician often fears to administer digitalis (p 854) when the drug is sorely indicated if the digitalization has already been started the necessary use of the drug may be discontinued if congestive gastric symptoms are interpreted as manifestations of overdosage

Gastric congestion does not yield to local therapy

GASTRIC VARICES

Because of the intimate anastomosis between esophageal and gastric veins a *portal obstruction* that produces *esophageal varices* (p 1728) induces similar changes in the channels of the cardia The gastric varices may rupture and produce *hematemesis* (p 1764) simulating gastric ulceration or malignancy (p 1814) The obvious feature of the portal obstruction (p 1960) should prevent diagnostic errors Local treatment is futile

LOCAL MANIFESTATIONS OF SYSTEMIC DISORDERS

Vascular Lesions
- Chronic Passive Congestion
- Gastric Varices
- Dieulafoy Ulcer
- Thrombosis of Gastric Vessels
- Arteriosclerotic Ulcer

The Stomach in Systemic Infections
The Stomach in Metabolic Disorders
The Stomach in Trauma and Toxism
The Stomach in Neurogenic and Psychosomatic Lesions
- Gastric Tabes
- Gastric Neuroses
- Peptic Ulcer

LOCAL LESIONS WITH OR WITHOUT SECONDARY SYSTEMIC CONSEQUENCES

Congenital Abnormalities
- Hypertrophic Pyloric Stenosis
- Hiatus Hernia
- Para-esophageal Hernia
- Eventration of the Diaphragm
- Herniation through Ligament of Treitz
- Cascade Stomach
- Polyps

Trauma
- Thermal Injury
- Chemical Injury
- Mechanical Injury
- Penetration and Perforation
- Obstruction (Hourglass Pyloric)
- Foreign Bodies
- Dilatation
- Gastroptosis
- Duodenal Ileus

Inflammation
- Gastritis
  - Acute Gastritis
  - Chronic Gastritis
  - Phlegmonous Gastritis
- Duodenitis
- Duodenal Diverticula

Neoplasms
- Benign
- Malignant
  - Carcinoma
  - Myxosarcoma

DIEULAFOY S EROSION

Isolated arterial changes in the gastric vessels occur with rarity Sudden brisk *hemorrhage* is occasionally observed from the erosion of a small artery without any appreciable lesion in the remaining coats of the stomach (Dieulafoy s erosion)

With persistent bleeding or exsanguination it may be necessary to open the stomach and cauterize or ligate the bleeding vessel Only in this way is the diagnosis established Following operation the patient is put on an *ulcer regimen* (p 1790)

THROMBOSIS OF GASTRIC VESSELS

Thrombosis of the gastric vessels may occur as part of a general arterial disturbance as in *periarteritis nodosa* (p 1027) A local ulceration may be produced The diagnosis and management are the same as for *peptic ulcer* (p 1784)

ARTERIOSCLEROTIC ULCER

With a generalized arteriosclerosis (p 976) *trophic ulceration* of the stomach probably occurs with greater frequency than is usually recognized

Clinical Manifestations —The onset of persistent *gastric distress* in an elderly patient is often the only clinical manifestation of the lesion Occasionally the herald symptom is a brisk hemorrhage with *hematemesis* or *melena* Compared to the ordinary peptic ulcer the arteriosclerotic variety

DIFFERENTIAL DIAGNOSIS OF

Hematemesis

Bleeding from the stomach may be the result of disturbances of gastric or extragastric origin Hematemesis first must be differentiated from the vomiting of swallowed blood which has entered the stomach secondarily following hemoptysis (p 2058) or epistaxis (p 2123) There should be little difficulty in the case of nosebleed since the history and physical examination clearly reveal the primary origin of the bleeding In hemoptysis however manifestations which point to pulmonary bleeding include prior respiratory symptoms or signs and the bright red appearance of the blood admixed with sputum and bubbles of air

	DIAGNOSTIC FEATURES
Esophageal	Foreign body instrumental penetration peptic esophagitis congenitally short esophagus, diaphragmatic herniation or carcinoma Check by x ray
Gastroduodenal	Following protracted vomiting from whatever cause with blood streaking rather than gross hematemesis Peptic ulcer with hunger pain and demonstrable defect by x ray (p 1780) Arteriosclerotic gastric ulcer with generalized vascular deterioration hyperacidity and x ray defect (p 1763) Gastric carcinoma with anacidity anorexia and filling defect (p 1814) Acute and chronic gastritis best recognized by gastroscopy (p 1808) Dieulafoy ulcer with acute hemorrhage but otherwise normal findings
Hepatic	In any instance of profound jaundice Particularly in chronic congestive splenomegaly (Banti s syndrome) with ascites In portal cirrhosis accompanied by esophageal varices and ascites In acute yellow atrophy with leucin and tyrosin crystals in urine and demonstrable shrinkage of liver
Circulatory	Rupture of esophageal varices in portal obstruction and portal hypertension In association with acute or chronic thrombosis of portal or splenic veins From rupture of aortic aneurysm into esophagus
Hemic	With hemorrhagic disease but especially hemophilia thrombocytopenic purpura leukemia scurvy vitamin K deficiency and hemorrhagic capillary toxicosis (Henoch s purpura) Check hemogram and bleeding and coagulation times (p 3692) Note mucosal and cutaneous purpuras (p 3423)
Infectious	In blackwater fever of malaria with plasmodia demonstrable in blood smears (p 507) In yellow fever with history of epidemic jaundice In cholera of epidemic proportion In severe or malignant scarlet fever or measles with characteristic exanthems (p 172)

CONTINUED

Toxic and Metabolic	Following ingestion of corrosive poisons In acute and chronic alcoholism With deficiencies of vitamins C and K producing scurvy and hemorrhagic disease of the newborn. Note therapeutic responses to cevitamic acid and menadione (p 630) As terminal manifestation in azotemia In all varieties of severe cholemia with jaundice and evidences of hepatic insufficiency

is less likely to produce typical manifestations of peptic ulcer (p 1783) It is more prone to bleed and more likely to resist treatment and recur

Diagnosis—The diagnosis of the arteriosclerotic ulcer is impeded by the fact that exhaustive examinations deplete the afflicted patient Stool examinations for the presence of *occult blood* (p 3728) while the patient is on a meat free diet provide the greatest information at the least risk If there is persistent bleeding it is necessary to subject the patient to *radiographic* examination with contrast media (p 3742) *Gastric analysis* revealing a *histamin anacidity* (p 3892) suggests the presence of a malignant lesion

The differential diagnosis from *peptic ulcer* is an academic discipline since both lesions are benign and require conservative medical treatment of a similar nature It is often impossible to be certain that a malignant process is not present *Gastroscopy (p 1745) and exploratory laparotomy* are performed with definite risk which is not worth while unless in the event a carcinoma is discovered the practitioner and his patient are prepared to face radical surgery (p 3997)

Treatment—In view of the formidable risk of surgery in a patient with advanced arteriosclerosis and the small prospect for long term survival or cure it is the better part of wisdom to institute conservative medical treatment as in peptic ulcer (p 1790) The practitioner errs if he enters into this decision without taking into his confidence some responsible member of the family or in certain instances the patient himself

Emergency Treatment of Hematemesis

The treatment of hematemesis may be conducted according to the following principles

1—Administer an opiate preferably dilaudid 2 mg (1/30 gr) to allay restlessness

2—Set up intravenous drip immediately giving 5 per cent dextrose in saline until plasma can be obtained

3—Obtain blood for grouping and continue plasma infusion until compatible donor can be located and bled then substitute citrated blood for plasma in the intravenous drip

4—Continue intravenous drip with 5 per cent dextrose and saline until evidences of active bleeding have ceased then begin cautious small feedings by Sippy (p 1791) or Meulengracht s method (p 667)

5—If bleeding continues summon the surgeon and consider operative interference

6—If there are evidences of acute gastric dilatation with retention of blood consider cautious passage of Levine tube for purposes of decompression

7—Attempt to allay anxiety by reassurance and the liberal administration of sedatives particularly barbiturates by addition of soluble preparations to the intravenous drip (p 3775)

THE STOMACH IN SYSTEMIC INFECTIONS

Many infectious diseases are associated with gastric dysfunction *Fever* itself inhibits gastric secretion and motility producing anorexia and delayed emptying In certain of the specific infections such as *scarlet fever* the early occurrence and persistence of vomiting suggest the presence of a true *gastritis* In other states such as *pneumococcus pneumonia* the toxemia tends to produce an ominous and treacherous *gastric dilatation*

SYPHILITIC GASTRITIS

Syphilis of the stomach is a very rare condition Before the modern era of chemotherapy in syphilis single and multiple gummas of the stomach were occasionally encountered The condition of "leather bottle" stomach (linitis plastica) was believed to be luetic in origin At the present time gummas are pathological curiosities rarely seen within the lifetime of a practitioner and linitis plastica is currently believed to be a scirrhous cancer (p 1815) The association of syphilis with peptic ulcer or malignancy is coincidental

Upon suspicion of the presence of a syphilitic gastritis the patient should be given vigorous antiluetic treatment particularly stressing the use of iodides (p 608)

OTHER SPECIFIC VARIETIES OF GASTRITIS

Tuberculosis and actinomycosis of the stomach (p 489) have been described These conditions are rarities and the diagnosis is made by histological section Occasionally, *hookworm* (p 1893) *tapeworm* (p 1893) or *ascaris lumbricoides* is encountered in the stomach or duodenum

THE STOMACH IN METABOLIC DISORDERS

The function of the stomach is deranged in almost every type of metabolic disorder The avitaminoses particularly pellagra and sprue produce inflammatory gastric changes similar to those observed in the oral cavity In primary anemia there is association of *atrophic gastritis* (p 1808) and *glossitis* (p 1707) the gastric disorder probably precedes the blood changes and may be in the nature of a causative mechanism Although therapy is eminently successful so far as the hematologic condition is concerned the gastritis is permanent

THE STOMACH IN TRAUMA AND TOXEMIA

Trauma and toxic factors such as burns and frost bites are causative mechanisms or at least provocative agencies in the production of certain types of *peptic ulcer* (p 1780) The appearance of digestive symptoms following the injury suggests the diagnosis

NEUROGENIC AND PSYCHOSOMATIC CONDITIONS

Gastric Tabes

The tabetic crisis characterized by violent pain and secretory disturb ances of the stomach is a manifestation of *syphilis of the spinal cord* (p 1464) Its intermittent character suggests that the neuritis may involve the constituents of the involuntary nervous system

Diagnosis—The pain of the tabetic crisis may simulate that of *angina* (p 890) *coronary occlusion* (p 983) *perforation* of a gastric ulcer or a *malignant* process The *differential diagnosis* rests on the findings of typi cal tabetic features in the patient the *pupils* are irregular and fixed the *knee jerks* are absent the *spinal fluid findings* leave no doubt as to the nature of the process (p 3734) *Coexistence of tabes and organic gastric disease* may give rise to difficulty Laboratory investigations particularly radiography should soon settle this point

Treatment—The symptomatic treatment of the tabetic crisis is most effectually carried out by intravenous injections of *thiamine chloride* (100 mg) in conjunction with specific therapy (p 1466)

The Gastric Neuroses

Functional disturbances of the stomach are of such frequent occur rence that it is doubtful whether any individual lives the span of his life without suffering at one time or another from some manifestation of this affliction The great American stomach on which hundreds of millions of dollars are spent annually for medication of one type or another is most often a *gastric protest* to the stress and strain of modern civilization Since it may also be a harbinger of serious organic disease it represents a symptom complex that challenges the practitioner every day of his life He is constantly haunted by persistent and recurrent symptoms that as sail the confidence of the patient in his therapeutic ability he is frequently shocked to learn that long standing belly ache was the expression or forerunner of a peptic ulcer a malignant gastric process or gallstones

Reflex Gastric Neuroses—Secretory and motor abnormalities of the stom ach and duodenum are frequently caused by organic disease of the bowel or the gallbladder These *reflex gastric neuroses* are differentiated from the purely functional states next to be discussed

Functional Gastric Neuroses—The functional gastric neuroses constitute local reactions to disturbances involving the psyche the personality or the involuntary nervous system either alone or in combination The reaction picture may be secretory motor sensory or mixed

Reflex Versus Functional Gastric Neuroses—The functional gastric neu rosis is differentiated from the reflex type by the method of exclusion The astute practitioner will not commit himself to the diagnosis of a functional state until he has dismissed the possibility of associated organic disease by frequent stool examinations *gastric analyses radiography* of the digestive tract and if necessary *gastroscopy* The investigation is incomplete if it omits radiography of the *gallbladder region* by a *scout film* (p 1988) and *cholecystography* (p 2000) Only this type of meticulous investigation prevents serious errors

The Varieties of Gastric Reaction—A rational concept of the gastric neu roses has been hampered by the practice of naming the clinical manifesta

tion and regarding the catalogued condition as a disease rather than a symptom or a symptom complex Thus the practitioner is confronted with a nomenclature that includes aerophagia, anorexia nervosa nervous indigestion nervous dyspepsia hyperacidity continuous gastrosuccorrhea and the like These constitute the sound and the fury of gastro enterology They *focus upon the gastric response rather than the etiologic factors and* mechanisms that provoke the reaction Such concepts serve as soporifics relative to gastric diagnosis and obstruct the preparation of an intelligent and successful therapeutic regimen

Glossary of Descriptive Terms —The following glossary of descriptive terms used in reference to gastric disturbances will serve for purposes of orientation

Achylia Gastrica

Achylia gastrica is a condition in which there is *neither acid nor peptic secretion* The gastric principle of hematopoiesis may be also absent but this is not a necessary accompaniment

This condition is seldom present from birth though a congenital or familial predisposition to its appearance may be present It is more frequent in families some of whose members have pernicious anemia The association of achylia gastrica with gastritis has been established by gastroscopic examination but achylia may be present with a normal mucosa

Achylia gastrica may be a reflection of an endocrine disturbance such as *hyperthyroidism* or of a nutritional disorder such as *vitamin B deficiency* it is also a symptomatic finding in *gastric cancer* and *primary hyperchromic anemia*

Aerophagia

Aerophagia refers to the habit of air swallowing usually associated with *burping* (belching) It is best seen in bottle-fed babies who upon completion of their feeding bring up a bubble of gas when patted on the back while placed over the mother's shoulder Contrary to the general opinion the belched gas is identical in chemical composition with atmospheric air Hence it is not a product of gastric fermentation and has no clinical significance Socially the fastidious regard the burp as an esthetic error although other people regard the habit as a salvo to culinary satisfaction

Anacidity

Anacidity indicates an *absence of hydrochloric acid secretion* from the stomach peptic activity is retained and ordinarily the injection of *histamine phosphate* (p 3391) produces an acid response Anacidity in itself is probably productive of few if any symptoms

Anorexia

Anorexia signifies lack of appetite (p 1779)

Anorexia Nervosa

Anorexia nervosa (p 1778) is a symptom complex that probably arises as a psychogenic disturbance but terminates with manifestations of deficiency in anterior pituitary and thyroid secretions It is not a gastric disease

Biliousness

Biliousness is a term that is much abused by the laity and copywriters for proprietary medications In a general way the term is meant to indicate feelings of malaise associated with errors in the gastro intestinal tract The implication of a hepatic dysfunction is unwarranted

Bulimia

Bulimia refers to excessive appetite (p 1776)

Cardiospasm

Cardiospasm is considered in the discussion of *Disturbances of the Esophagus* (p 1721)

Ep gastric Fulln ss

Fullness *after meals* is a normal expectancy when excessive amounts of food ha e been eaten beyond stomach capacity It also occurs from boltin, food so rapidly that the gastr c tonus has not time to relax and accommodate itself to the altered con litions Fu lne s *before meals* suggests gastric retention hypersecretion or the reverse peristalsis syndrome (p 1 78)

Gastre tas s

D latation of the stomach (gastrectasis) is not synonymous with atony though they may be associated It refers to the enlargement of the gastric capacity It may be *acute* as particularly seen following operation (p 4012) and in the acute febrile d eases such as pneumonia (p 2177) *Chronic d latat on* occurs with pyloric obstruct on and other organic disturbances

Gastr c Atony

Atony of the stomach refers to a loss of gastric muscle tone such as occurs in the febrile states in cl ron c debilitating disease and especially with ptosis

Hyperac d ty

Hyperacidity is the most abused gastric diagnosis The outpouring of a consid rable quantity of hydrochloric acid may be transitory or prolonged Like sali at on it may result from psychic st mulation or the presence of a local irritant The find ng of high titratable acidity in the stomach is compatible with complete gastric comfort The clin cal problem that arises requ res elucidation of the cause of the hyperac d ty therapy is aimed at its control or elimination

Hyp rsecret on Hypermyxor*hea and Succorrhea*

Hypermyxorrhea or gastric succorrhea (Reichman s Disease) refers to an outpour ng of gastric mucus This reflex mechanism is not a pathological condition but a response to irritation

Hypo ac d ty and S bac d ty

Hypo-acid ty and subacidity refer to dimin shed secretion of hydrochlor c acid and gastric mucus It is doubtful whether these conditions are productive of significant sympto ns

Nausea

Nausea (p 17 0) precedes vom ting and is a common manifestat on of *reve se peris talsis* It more often results from extragastric than from gastric d sturbances

N rvo s Dyspeps a

Nervous dyspeps a is a descripti e term employed by the laity and refers to any of the gastr c neuroses (p 1767)

Nervous Ind gest on

Nervous indigestion is a descriptive term that is most confusing and usually refers to a hypersthenic gastric neurosis (p 1 73)

N r ous Vom t g

Nervous vomiting is a descriptive term that has no clinical significance or utility

P stalt Unrest

Peristaltic unrest is a d scr pti e term that refers to hypersthen c states (p 1 3)

P ca (Parorex a)

Pica (parorex a) and eating a perverted appetite is a symptom *usually of neurotic or* psychogenic s gn ficance (p 1544)

Pylo ospasm

Pyloro p sm *is symptomatic* distu bance *in the newborn* whi h may *lead to* protra te l *persistent or cycl c vom ting In a lults it is a* man festat on *of* incre ed tonus of the *sphincter* m chanism

Py o s (H artbu)

Pyros s or heartburn is a sensation of burning in the retrosternal region which is not d agnostic of hyperacidity It may occur w th a variety of d sturbances i clu ing a hl hydria (p 3725)

tion and regarding the catalogued condition as a disease rather than a symptom or a symptom complex Thus the practitioner is confronted with a nomenclature that includes aerophagia, anorexia nervosa nervous indigestion nervous dyspepsia hyperacidity continuous gastrosuccorrhea and the like These constitute the sound and the fury of gastro enterology They focus upon the gastric response rather than the etiologic factors and mechanisms that provoke the reaction Such concepts serve as soporifics relative to gastric diagnosis and obstruct the preparation of an intelligent and successful therapeutic regimen

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Fullness *after meals* is a normal expectancy when excessive amounts of food have been eaten beyond stomach capacity. It also occurs from bolting food so rapidly that the gastric tonus has not time to relax and accommodate itself to the altered conditions. Fullness *before meals* suggests gastric retention, hypersecretion or the reverse peristalsis syndrome (p 1778)

Gastrectasis

Dilatation of the stomach (gastrectasis) is not synonymous with atony though they may be associated. It refers to the enlargement of the gastric capacity. It may be *acute* as particularly seen following operation (p 4012) and in the acute febrile diseases such as pneumonia (p 2177). *Chronic dilatation* occurs with pyloric obstruction and other organic disturbances

Gastric Atony

Atony of the stomach refers to a loss of gastric muscle tone such as occurs in the febrile states, in chronic debilitating disease and especially with ptosis

Hyperacidity

Hyperacidity is the most abused gastric diagnosis. The outpouring of a considerable quantity of hydrochloric acid may be transitory or prolonged. Like salivation it may result from psychic stimulation or the presence of a local irritant. The finding of high titratable acidity in the stomach is compatible with complete gastric comfort. The clinical problem that *arises requires elucidation of the cause of the hyperacidity*; therapy is aimed at its control or elimination

Hypersecretion, Hypermyxorrhea and Succorrhea

Hypermyxorrhea or gastric succorrhea (Reichmann's Disease) refers to an outpouring of gastric mucus. This reflex mechanism is not a pathological condition but a response to irritation

Hypoacidity and Subacidity

Hypo-acidity and subacidity refer to diminished secretion of hydrochloric acid and gastric mucus. It is doubtful whether these conditions are productive of significant symptoms

Nausea

Nausea (p 1770) precedes vomiting and is a common manifestation of *reflex eye strain*. It more often results from extragastric than from gastric disturbances

Nervous Dyspepsia

Nervous dyspepsia is a descriptive term employed by the laity and refers to any of the gastric neuroses (p 1767)

Nervous Indigestion

Nervous indigestion is a descriptive term that is most confusing and usually refers to a *hypersthenic gastric neurosis* (p 1773)

Nervous Vomiting

Nervous vomiting is a descriptive term that has no clinical significance or utility

Peristaltic Unrest

Peristaltic unrest is a descriptive term that refers to hypersthenic states (p 1773)

Pica (Parorexia)

Pica (parorexia) indicating a perverted appetite is a symptom usually of neurotic or psychogenic significance (p 1344)

Pylorospasm

Pylorospasm is symptomatic disturbance in the newborn which may lead to protracted *persistent or cyclic vomiting*. In adults it is a manifestation of increased tonus of the *splanchnic mechanism*

Pyrosis (Heartburn)

Pyrosis or heartburn is a sensation of burning in the retrosternal region which is *not* diagnostic of hyperacidity. It may occur with a variety of disturbances including achlorhydria (p 3725)

DIFFERENTIAL DIAGNOSIS OF

Dyspepsia (Indigestion)

The terms dyspepsia and indigestion are used as catch alls to embrace all of the upper digestive disturbances including nausea vomiting regurgitation heart burn, belching merycism rumination gastralgia and gastrectasis In general indigestion may be du to digestive or extra alimentary causation Diagnostic investigations often must go far afield to discover the etiologic mechanism Therapeutic efforts to be successful mu t embrace measures that aim beyond the digestive tract

	DIAGNOSTIC FEATURES
Psychogenic	Poor food bad cooking slovenly service Emotional characterologic and situational disorders Hypersthenic and hyposthenic gastrointestinal neuroses Diagnose by exclusion after survey to include x ray examinations of digestive and biliary tracts (p 2000)
Neurogenic	With increased intracranial tension from whatever cause Supplement neurologic examination with x rays of skull and examination of cerebrospinal fluid (p 3734) migraine and epilepsy
Pharmacologic	Following the use of analgesic antipyretics digitalis sulfonamides quinine iodide salicylate antimony mustard, emetics apomorphine opiates picrotoxin and general anesthetic
Toxicologic	In association with alcoholism and drug addiction With poisoning due to lead mercury bismuth and arsenic From exce sive use of tobacco With food poi onings particularly those caused by staphylococcus toxin.
Fever	With any pyrexia beyond 102 F In low-grade fevers a sociated with tuberculosis
Cachexia	Especially with malignancies of the digestive tract Diagnostic survey to include x ray series (p 3742) and examinations of stool for occult blood (p 3728)
Generalized Infections	In all febrile states but particularly those as ociated with diarrhea and hyperpyrexia Particularly with tuberculosis and syphilis of the central nervous system
Metabolic	In early pregnancy With cyclic vomiting and acidosis in infancy With acidosis azotemia cholemia avitaminoses adrenal cortical deficiency thyrotoxic crises migraine epilepsy and anorexia nervosa Make complete examinations of urine and blood (p 3692) Check B M R
Allergy	Particularly after ingestion of common allergens such as milk, eggs wheat and pork
Oropharyngeal	With local disturbances productive of anorexia

CONTINUED

Upper Digestive Tract	From over-eating and gluttony In as ociation with esophagitis cardiospasm and malignancy of the gullet demonstrable by x ray or gas troscopy (p 1745) With *congenital hyper trophic tenosis* gastric neuroses peptic ulcer gastric retention acute and chronic gastritis gastroptosis and gastric malignancies Make complete survey to include gastric analysis x ray series and gastroscopy if necessary (p 1745)
Intestinal	With intestinal neuroses associated with con stipation or diarrhea With specific and non specific entero-colitis appendicitis intestinal obstruction and disturbances of the rectum and anus Supplement physical examination with survey of stool (p 3727) x ray series (p 3742) and sigmoidoscopy (p 1907)
Helminthiasis	Particularly with tape worms and hook worms Examine stools for ova and parasite (p 1893) Note eosinophilia (p 542)
Hepatobiliary	With hepatitis chronic passive conge tion of the liver hepatic cirrhosi cholelithiasis and cholecystitis Make complete survey to include examinations of duod nal contents and blood and cholecy tograms (p 2000)
Circulatory	With backward failure With coronary throm bosis coronary insufficiency and angina pec toris as differentiated by electrocardiography (p 803) In hypert nsive encephalopathy with chang s in fundus oculi and azotemia (p 2276)
Hemic	With secondary and primary anemias Note hemogram and therapeutic response to hemat inics and liver extract (p 1049)
Resp ratory	With all types of nasal obstruction With lung abscess Obtain x rays of acces ory sinuses and lung field
Renal	In all chronic nephropathies with retention of nitrogenous products and impairment of renal function In calculus disease particularly with impaction Make x ray survey and refer to urologist for cy toscopy (p 2248)
Ocular	Particularly with eye strain and glaucoma Refer to ophthalmologi t for refraction and measurements of intraocular tension
Labyrinthine	With acute and chronic labyrinthitis Ménière s syndrome mastoiditis petro itis and sea sick ness Refer to otologi t for labyrinthine test and audiometry
Peritoneal	With a cites In all types of acute and chronic peritonitis Con ider abdominal puncture (p 1825)
Pancreatic	Particularly with insufficiency c us ng steator rhea

Reg g tat on (W t r Brash)

Regurgitation (water brash) denotes a painless return of gastric cor tents to the mouth It often occurs during the belch As oppos d to pyrosis the regurgitated material cau es

no burning or distress Regurgitation is one of the manifestations of the *reverse peristaltic syndrome* (p 1778)

Rumination (Merycism)

Rumination and merycism are descriptive terms referring to the regurgitation of food from the gastric cavity as practiced in animals This condition is usually exhibited by psychopaths and has no relationship to gastric disease (p 1364)

Singultus (Hiccough)

Singultus (hiccough) results from a spasm of the diaphragm through irritation of the *phrenic nerve* It differs from belching in that the former is more or less voluntary while the hiccough is involuntary and cannot be discontinued by any act of the will See *Hiccough* (p 1933)

Vomiting

Vomiting (p 1770) is the result of a most complicated mechanism centrally it is controlled *in the medulla close to the region which governs respiration* In the limited gastric sense it is a result of *reverse peristalsis* (p 1778) and may be a symptom of minor or of the gravest significance Recurrent and persistent vomitings lead to *dehydration* with a disturbance in the electrolyte pattern toward the side of *alkalosis* since gastric acid is lost in the vomitus

Pathogenesis of Functional Gastric Neurosis—The production of the functional gastric neurosis requires the mediation of cerebrum or psyche in voluntary nervous system and end organ in the gastric glands or gastric musculature The neurosis may be caused by a disturbance of any or all of these constituent parts

The Psychic Factor—Gastric neuroses are produced by a variety of psychic disturbances Visual observations with the gastroscope permitting direct examination of the gastric mucosa attest to the delicate response of the stomach to emotional stimuli Mucus and acid are poured forth in tremendous quantities and vascular changes occur in the nature of congestion or ischemia Motor activity is suppressed or activated depending on diverse factors

In the susceptible subject great joy is as apt to precipitate a disturbance as sorrow or anxiety Psychiatrists have sought to establish that the nature of the psychogenic disturbance determines the type of the gastric response This hypothesis is relatively unimportant for the practitioner It is sufficient for him to recognize that acute and chronic emotional disturbances affect the stomach whatever may be the type of response Certain patients under great strain develop complete *anorexia* while others cannot satisfy their appetites and grow fat on worry Excitable children often vomit on the slightest excuse and become conditioned to emesis in many ways

Most functional gastric disturbances are psychogenic The practitioner who fails to recognize this principle and treats the stomach instead of the patient can expect only disappointment and humiliation for his efforts

The Role of the Involuntary Nervous System—The pathway that connects end organ and psyche is the involuntary nervous system (p 1388) The craniosacral (*cholinergic*) and thoraco lumbar (*adrenergic*) subdivisions are mutually antagonistic regarding most gastric functions Stimulation of the vagus produces many of the manifestations of *hypersthenic gastric neurosis* (p 1395) The administration of the depressants of the vagal system reduces secretion and motility but not to the degree that is gener

ally believed The antagonistic *thoracolumbar system* has much less appreciable effect on the stomach, the pharmacological manifestations are feeble and have little clinical importance stimulants such as epinephrine produce effects resembling the actions of depressants of the antagonistic cholinergic subdivision (belladonna) Hence epinephrine and related amines have been used in the treatment of hypersthenic neurosis by those who do not realize that the effects are quantitatively too feeble and transitory to be of any therapeutic value

AUTONOMIC IMBALANCE —With the gastric neuroses there are often associated abnormalities of the vasodermal system heart rate and smooth muscle elsewhere in the body Autonomic imbalance (p 1395) is often encountered in the gastric neuroses but there is never the pure *vagotonia* or *sympathicotonia* as has been suggested by Viennese clinicians The manifestations are always mixed they may be partially cholinergic and partially adrenergic such as bradycardia with clammy hands and feet

The recognition of the role of the involuntary nervous system in the gastric neuroses stresses the widespread nature of the etiologic and pathogenic mechanisms involved It emphasizes the necessity of treating the patient instead of the end organ

End Organ Response (*Reaction Picture*) —One of the fascinating features of the gastric neurosis is its individual pattern Most patients who suffer from this condition can predict the expected symptoms with surprising accuracy The gastric reaction picture is fixed and as characteristic for the individual as the fingerprint

The type of gastric neurosis depends somewhat upon the constitutional factor The stomach of the steer horn type is more apt to exhibit hyperacidity hypermotility and spasm while the fish hook stomach is prone to be low in gastric secretion tonicity and motility

What determines the individual reaction picture remains at the present time an unsolved problem Students of *psychiatry* suggest the possibility that the response is determined by the nature of emotional disturbances Those whose main interest is the *involuntary nervous system* regard the antagonism between the subdivisions as the determinant The *morphologist* emphasizes the physical and anatomical factors which hold least manna for the therapist *Endocrinologists* stress the greater frequency of sthenic symptoms in the male and attribute these to a dislocation of the androgen/estrogen ratio

Clinical Varieties —The clinical classification of gastric neuroses is simplified by reducing their numbers to the basic types of hypersthenic and hyposthenic manifestations and the syndrome of reverse peristalsis Most often the patient presents a combination of the features of each

HYPERSTHENIC GASTRIC NEUROSIS

The hypersthenic gastric neurosis may be motor secretory or combined The *secretory states* include hypersecretion hyperacidity hypermyxorrhea and continuous gastrosuccorrhea (Reichmann s disease) The *motor accompaniments* include hypermotility hyperkinesis (peristaltic unrest) gastrospasm pylorospasm and cardiospasm For the most part the hypersthenic manifestations are the equivalent of stimulation of the cholinergic system as produced pharmacologically by physostigmine

Clinical Manifestations—The digestive symptoms of the hypersthenic gastric neurosis are varied and diverse The reaction picture is usually characteristic for each patient and consists of any one of a variety of complaints relative to the physiological disturbance Most often the patient notes *nervous dyspepsia* or *nervous indigestion* Many patients complain of a syndrome that closely simulates that of *peptic ulcer* (p 1780) There may be bulimia absence of a feeling of satiety after meals epigastric distress hunger pains and relief from the ingestion of food Often *hypersthenic symptoms are associated with those of the reverse peristalsis* syndrome There are thus added to the other discomforts belching regurgitation with heartburn pyrosis nausea and vomiting

The symptoms of the gastric neurosis tend to abate and recur usually in relationship to fatigue or some psychic insult During the period of exacerbation distress follows the ingestion of almost any food but most particularly those that are spiced highly seasoned fried, or mechanically rough Alcohol produces severe distress and even tobacco cannot be enjoyed During the periods of freedom from symptoms previously noxious substances can be ingested with gratification The transition from the functional neurosis to peptic ulceration may be imperceptible and may come as a great surprise to the practitioner who has taken for granted the nonorganic nature of the affliction

Physical Examination—Physical examination of the patient with the gastric neurosis yields little positive information regarding the subjective complaint Usually evidences of other disturbances in the realm of the involuntary nervous system are found Most often these are of a mixed nature with vagotonia predominating The patient often has a *slow pulse rate* and it is not uncommon to find a *lowered metabolic rate* (p 719) The concept of a pure ' vagotonia is usually upset by a *vasodermal manifestation* which includes cold and moist clammy hands and feet acrocyanosis and marked susceptibility to cold A physical finding that is *prone to give the practitioner some uneasiness is the* palpability of the *spastic gut* Usually this is rolled under the examining finger as a tender freely movable sausage' located in the right or left lower quadrants or both The suspicion of a neoplasm arises and is often not allayed until radiography and stool examinations have been completed

Laboratory Examinations—Hypersthenic gastric neuroses are diagnosed on the secretory side by the gastric test meal for motor manifestations recourse to radiography is warranted

Diagnosis—The functional hypersthenic gastric neurosis must be differentiated from the *reflex neurosis* secondary to peptic ulcer or a diseased gallbladder In the interests of accuracy for his own self protection and as a type of psychotherapy for the anxious patient the practitioner should insist upon a *complete radiographic study* and frequent stool examinations for occult blood Specimens are obtained after a meat free diet for three days and are examined successively for another period of three days Radiographic studies include a *barium meal* a *scout film* of the abdomen particularly a postero-anterior view focused over the gallbladder region and *cholecystography* (p 2000) It is well to remember that a dated examination does not hold for all time if symptoms persist alter in quality or intensity and fail to respond to usual therapy *reexamination* is required

Treatment—The management of the patient with a hypersthenic functional gastric neurosis is directed at the psyche the vagal portion of the involuntary nervous system and the end organ in the stomach

Psychotherapy—Psychotherapy requires that the physician obtain a complete history of the way of life If necessary a *diary history* (p 3474) is requested so that the practitioner may be acquainted with the circumstances of the patient s outer and inner life

In so far as is possible the causative factors are eliminated Although it is usually impossible to alter all *characterological and situational difficulties* in any human life the recognition of the relationship is often a helpful measure The psychological aspects of therapy are completed by acquainting the patient with the usual *course of the disease* the possibility of *recurrence* under provocation is emphasized progression toward *organic disease* particularly peptic ulcer is stressed as an additional argument for the patient to adhere to a routine

Sedation—Sedation by phenobarbital particularly in the form of Mistura Nigra (p 1757) is productive of the greatest benefit *Hypnotics* of the barbiturate group (p 3839) are given each night for a few weeks to produce a quiet and restful sleep Persistence of symptoms suggests the need of a vacation or of a rest cure at home or in the hospital

Cholinergic Depression—Since the majority of the symptoms of the hypersthenic neurosis *correspond to stimulation of the vagus nerve* the administration of *belladonna* or one of the newer synthetics such as *Syntropan* (p 3875) or *Novatropine* is recommended Unfortunately these preparations are of greater pharmacologic significance than therapeutic efficacy Occasionally a patient obtains relief from their use but more often they seem to accomplish much less than is anticipated It is wise to give the belladonna derivative in pure form Only in this way can the dosage be regulated to the individual need Tincture of Belladonna for example is given in increasing doses until there is considerable dryness of the mouth To obtain this may require anywhere from 1 to 2 cc three times daily Additionally the effects of anti histamine products notably pyribenzamine (p 565) in doses of 50 to 100 mg may be employed after meals and at bedtime

A popular tablet which combines belladonna and phenobarbital action is written as follows

℞	Atropine Sulfate	0 015
	Sodium Phenobarbital	0 [illegible]5
	Sodium Bicarbonate	q s

Divide and make 15 tablets or capsules
S g One after meals and at bed time
In this prescription atropine may be replaced by novatropine using a total amount of 0 03 [illegible] o syntropan 0 75 gm

Antacids and Protectives—The local gastric manifestations of the neurosis are best relieved by the use of nonabsorbable chemical antacids particularly *magnesium salts* (p 1754) or physical antacids of the *aluminum* type (p 1755) *Gastric mucin* (p 1756) also functions as a protective and can be included in the routine

Combined Drug Therapy—The combined drug therapy of the hyper

sthenic gastric neurosis is best integrated by giving the *belladonna preparation* before each meal, *Mistura Nigra* after meals and the antacid mid way between meals and at bedtime The last dose of the antacid is combined with the *hypnotic*

Hospitalization —A period of hospitalization is often of the greatest value when obstinate symptoms or manifestations are encountered and for all patients who can afford to "gild their infirmity

Dietotherapy —Other than the prescription of a *bland smooth regimen* (p 606) dietotherapy plays an unimportant role in the management of the hypersthenic states The patient's eating habits are determined and a routine is suggested that fits in with the usual diet Frequent small meals

DIFFERENTIAL DIAGNOSIS OF

Polyphagia, Bulimia and Pica

Polyphagia refers to frequent feedings without necessary increase in caloric intake With bulimia there is excessive appetite that usually results in obesity unless there is present some associated metabolic disorder such as diabetes mellitus Pica is the condition of perverted appetite most often of psychogenic origin but occasionally dependent upon dietary imbalance

	DIAGNOSTIC FEATURES
Psychogenic	Nervousness Sexual frustration Hysteria Expansive psychoses
Digestive Disturbances	In association with hyperperistalsis hypersecretion and peptic ulcer Supplement physical examination and gastric analyses with barium x rays (p 3742)
Helminthiasis	Usually the result of avitaminoses and anemias associated with worms Examine stools for ova and parasites (p 1893) Note eosinophilia and secondary anemia in hemogram (p 3704)
Metabolic	Normal growth Pregnancy Diabetes mellitus with glycosuria and hyperglycemia due to hypoinsulinism In association also with hyperinsulinism and hypoglycemia often due to adenomas of the pancreas. In diabetes insipidus with polydipsia and polyuria In hyperthyroidism with elevation of B M R and therapeutic response to iodide

are preferable to the ordinary three meals a day In between feedings are comforting as in peptic ulcer Spices condiments alcohol coffee tobacco raw and uncooked food and roughage are interdicted

Bowels —The care of the bowels requires only *training in normal hygiene* so that an evacuation is accomplished before or after breakfast Cathartics are avoided Often the ingestion of a cup of warm water with a teaspoonful of bicarbonate of soda on arising is sufficient to induce a satisfactory evacuation

General Hygiene —The general hygiene of life should be improved patients are encouraged to take vigorous walks and outdoor exercise Great comfort is afforded by the application of heat to the abdomen in the form of a hot water bottle or an electric pad

HYPOSTHENIC GASTRIC NEUROSES

The hyposthenic gastric neuroses correspond to the manifestations produced by inhibition or paralysis of the cholinergic system (vagus)

Clinical Manifestations—Hyposthenic gastric neuroses rarely cause the distress occasioned by the sthenic variety Most often the patient notes *lack of appetite* and a *dragging sense* in the epigastrium Usually these are combined with the reverse peristalsis syndrome and the patient adds regurgitation nausea and vomiting to the symptom complex Despite the low acid figures there may be pyrosis as well as simple water brash

Physical Examination—The physical examination in the hyposthenic states reveals little that is important The manifestations of the autonomic imbalance are less pronounced than in the sthenic neurosis the digestive symptoms often are associated with hypotension and *ptosis* the pelvic position of the stomach produces epigastric retraction with fullness in the hypogastric region

Laboratory Findings—The important laboratory finding is the diminution or the absence of free acid in the stomach contents histamine usually but not invariably produces an acid response Roentgen studies confirm the accompanying ptosis which often results in sharp angulation in the pyloric and duodenojejunal regions

Diagnosis.—With histamine anacidity the hyposthenic states require a diagnostic investigation to rule out gastric cancer and primary anemia *Radiographic* and in unusual circumstances *gastroscopic* surveys of the upper digestive tract are required to demonstrate or rule out the insidious onset of malignancy The *hemogram* is needed for early recognition of a primary anemia which may have an asymptomatic stage lasting many years *Bone marrow smears* (p 1043) may reveal evidences of pernicious anemia before changes are observed in the capillary blood

In the presence of additional symptoms *reexaminations* are advisable if malignancy is still suspected an *exploratory laparotomy* may be required

Course—Because of the possible development of blood changes or of malignant process in the stomach the patient is required to report at frequent intervals for examination Fortunately the majority of patients live the span of their lives without significant disturbances from the gastric condition

Treatment—Psychotherapy and administration of acid constitute the main reliance in the treatment of hypo thenic gastric neuroses

Psychotherapy—Psychogenic factors and disturbances of the involuntary nervous system are much less manifest in hyposthenic states than in hypersthenic gastric neuroses Nevertheless the same types of investigation and therapy are required (p 1774)

Autonomic Drugs—There is no effective way of stimulating acid production Injections of *histamine* (p 3890) cause untoward symptoms of an unpleasant nature that far outweigh possible therapeutic benefits

Acid—A most important therapeutic endeavor is the administration of *hydrochloric acid* (p 1740) While many clinicians doubt the occurrence of gastrogenous diarrhea which results from absent acidity a certain number of patients experience definite relief when acid drops are given consistently and in large quantity

The acid is best taken through a glass tube before and during meals 1 to 2 cc are diluted in one quarter to one half glass of water flavored with the juice of a lemon or an orange One dose is taken before meals and another is sipped throughout the meal so that a daily total of 6 to 12 cc is ingested This is relatively little compared to the 500 cc normally secreted by the stomach Patients who object to the nuisance of acid drops may take the more expensive capsules of glutamic acid (p 1740)

Systemic Therapy—The general condition is bettered by *outdoor exercise* particularly walking *rest after meals* and the use of *sedatives* and *hypnotics* as in the hypersthenic states (p 1775) Patients who have a ptosis should be encouraged to do *abdominal exercises* (p 3758) and often profit by the use of a fitted *support*

REVERSE PERISTALSIS SYNDROME

The classical work of Alvarez called attention to the grouping of a variety of gastric disturbances on the basis of reverse peristalsis In the reverse peristalsis syndrome the likely causative mechanism is a disturbance in the *forward gradient* of peristalsis a back wash occurs much in the manner of an undertow observed at a bathing beach

Clinical Manifestations—The symptoms of reverse peristalsis include belching fullness bloating regurgitation water brash pyrosis heart burn nausea and vomiting With these are associated more often the hypersthenic symptoms less frequently the hyposthenic variety They may be reflex to gallbladder disease

Laboratory Examinations—The syndrome of reverse peristalsis yields no *significant laboratory data other than the appearance* of retroperistalsis in the contrast radiograph

Diagnosis—It is imperative to differentiate between functional reverse peristalsis and the syndrome of organic obstruction (p 1873) Hence the diagnosis is deferred until radiography has proved the integrity of the gastric and intestinal lumen and the gastric test meal reveals no suspicion or evidence of retention (p 3721)

Treatment—The treatment of the syndrome of reverse peristalsis follows that outlined for other gastric neuroses Psychogenic factors are investigated Occasionally reverse waves result from irritation of the colon by rough gastric residue or constipated stools

In addition to therapy aimed at hypersthenic or hyposthenic symptoms the use of stomachics appetizers condiments and gastric tonics may correct the disturbance in the peristaltic gradient The popularity of chewing gum after dinner liqueurs particularly those flavored with peppermint and the ingestion of mint after meals attest to the value of these simple therapeutic measures

Symptomatic Treatment of Anorexia

The treatment of anorexia is directed first at the elimination of causative mechanisms Symptomatic measures may be useful for supplementation of specific measures

1 —Revision of menus to include palatable food tastily prepared and cleanly served

DIFFERENTIAL DIAGNOSIS OF

Anorexia

The sensation of appetite is dependent upon psychogenic physiologic and biochemical influences Loss of appetite may be due to bad food, poor cooking slovenly service or emotional disturbances *Anorexia also accompanies gastric hypotonicity and hyposecretion* Biochemical factors which reduce appetite include lowering of the basal metabolic rate and vitamin deficiency states

	DIAGNOSTIC FEATURES
Psychogenic Influences	Poor food. Bad cooking Slovenly service Emotional disturbance Characterological and situational conduct disorders particularly in infancy and childhood. Neurasthenia Hysteria The depressive psychoses Anorexia nervosa Consult psychiatrist for psychometry and therapy (p 1316)
Mechanical Disturbances	Edentia Ill fitting dentures Dental caries Gastric retention Constipation. Tympanites Ascites Ptosis Post nasal drip and nasal occlusion.
Local Inflammations	Cheilitis stomatitis gingivitis, glossitis and pharyngitis Rhinitis nasal accessory sinusitis tonsillitis, laryngitis and retropharyngeal or peritonsillar abscess Esophagitis gastritis enterocolitis peritonitis and fecal fistulas Lung abscess
Pain	Of all types with the exception of the hunger pain of peptic ulcer
Fever	In all conditions when rectal temperature exceeds 102° F With low-grade pyrexia particularly in tuberculosis
Cachexia	Particularly malignancies of the digestive tract Supplement physical examination with x ray survey (p 1740)
Pharmacologic	Following atropine amphetamine sulfate (Benzedrine) digitalis iodide salicylate quinine ipecac and the opiates
Generalized Infections	In association with fever With afebrile infections particularly tuberculosis
Endocrinopathies	Adrenal cortical deficiencies with pigmentation and hypotension Pituitary cachexias with low B M.R and marked emaciation
Metabolic	In achylia gastrica with therapeutic response to hydrochloric acid. In avitaminosis with therapeutic response to constituents of vitamin B complex In early pregnancy
Neurogenic	In association with dysphagia due to facial or bulbar palsies
Circulatory	In backward failure with chronic passive congestion of stomach and liver
Hemic	With primary and secondary anemias Note hemogram and responses to hydrochloric acid hematinics and liver extract (p 1049)

2 —Elimination of emotional strain at least at table Avoidance of nagging of children and of overemphasis on table manners
3 —Judicious use of condiments such as catsup mustard and spices
4 —Prescription of appetizer before meals consisting of sherry or a cocktail of gin or whisky
5 —Use of wine at meals
6 —Post prandial carminative in the form of peppermint candy for children or of a mint liqueur for adults
7 —Therapeutic trial with dilute hydrochloric acid before meals whether or not achylia exists
8 —Abdominal support in gastroptosis
9 —Recumbency with application of heat to abdomen in gastric hypotonicity
10 —Injections of insulin in doses of 5 to 10 units fifteen minutes before meals when simpler measures fail
11 —Supplementary use of multi vitamin preparations for therapeutic test

PEPTIC ULCER

The problems incidental to peptic ulcer afford a formidable challenge to the practitioner If regarded as a local lesion of the intestinal mucous membrane peptic ulcer is a mysterious ailment whose management is thoroughly unsatisfactory Considered from the broad viewpoint of a *psychosomatic manifestation* (p 1344) in which organic disease is engrafted upon or secondary to a preexistent gastric neurosis (p 1767), the problem becomes clarified The patient then may be successfully managed on a rational and intelligent basis

Pathogenesis of Ulcer—Investigation of the origin and mechanism by which peptic ulcer is produced and perpetuated resolves itself into two inquiries The first question involves the factors that produce the ulcer while the second pertains to those influences which prevent it from healing

Predisposition—There is unanimity of opinion relative to the presence of a predisposition to peptic ulcer though it is admitted that the predisposition is not diagnostic or pathognomonic Many patients exhibit features of the predisposition but have no ulcer A small minority of ulcer patients seem free from the manifestations of the predisposition The recognition of predisposition is of importance to the clinician in that it emphasizes the concept that the local lesion is a peripheral manifestation of some widespread disturbance

The predispositional features are constitutional emotional vegetative and hormonal

CONSTITUTIONAL—The constitutional features of peptic ulcer are least useful to the therapist the ulcerous patient may be of the *ptotic* or *sthenic* habitus (p 3490) the stomach is usually of the *steer horn* type but may be *fish hook* (p 174?) Perhaps the most characteristic feature in the facies is the depth of the *nasolabial folds* which cut furrows into the face The anthropometric data relative to palatal arch teeth and measurements of height width and breadth contribute little to the diagnosis or understanding of the syndrome

EMOTIONAL—Emotionally ulcerous patients seem more clearly to fit into a series of panels These patients are often tense and highstrung but outwardly controlled they perform work under great tension they are ambitious and often of the perfectionist type More often than not the ulcer patient is one whose mental characteristics have gained him a sedentary rather than a manual occupation Under these circumstances his muscles become flabbier while his cerebral activities are more involved and more exacting Continued success brings greater acclaim and more bellyache failure is intolerable to the point that the sufferer fulfills accurately the description of the saying that he is "eating himself up"

Suggestive corroboration of the neurogenic influence is afforded from experimental studies in which it was found that gastric ulceration followed injury to the *hypothalamus*

Additional evidence of the importance of the psychosomatic mechanism is afforded from broader biological inquiry Peptic ulcer seems to be a condition that is limited in its occurrence to civilized man It almost never occurs spontaneously in the lower animals It is difficult to produce experimentally by conditions that would in any way simulate those of the clinic

Certainly initiation of the peptic ulcer resides in some type of psychic or emotional insult The second phase is probably a disturbance in the realm of the involuntary nervous system setting in motion th secretory muscular or trophic features by which the local lesion is finally produced

VEGETATIVE —The victim of a peptic ulcer presents manifestations of a widespread disturbance in the *involuntary nervous system* (autonomic imbalance) There is usually an obvious vasomotor instability recognized as cold and clammy hands and feet and a tendency to blush and flush Often there is an associ ted bradycardia suggesting increased vagal tonus Prior to deve'opment of the ul er the patient gives evidences of previous hypersthenic funct onal disturbances of the gastro-intestinal tract involving not only the stomach but oft n the large bowel particularly the s gmo d

HORMONAL —The hormonal factor has been suggested by the male preponderance of ulceration *Androgen estrogen* ratios appear dislocated toward th male s de in many pati nts The inevitable sugge tion of estrogen therapy is under scrutiny *Enterogastrone* therapy how ver promises to reduce gastric secretion and diminish mot lity both experimentally (p 18 1) and cl nically

Summary —The recognition of psychogen c and vegetative influences in the predisposition to peptic ulcer is not a mere academic *exercise* it stresses the *importance of including* in the therapeutic regimen measures aimed at treating the patient rather than his stomach If the individual is treated correctly the ulcer will heal treatment of the ulcer and neglect of tl e pat ent gives l ttle promise of a successful therapeutic issue

E c t ng Causes —There are a number of demonstrable exciting causes of peptic ulcer In all l kelihood no one of th se produces the lesion without the presence of the predisposing circumstances

Hydrochloric Acid and Pepsin —It is as yet not known why hydrochloric acid and pepsin fa l to effect autod gestion of the stomach While excess ve secretions of acid and enzyme are not s fficient of themselves to produce ulcerations hyperac d ty *must be an important* exciting factor in the perpetuation of ulcer

Vascular Factors —Vas ular influences sometimes produce a *trophic ulcer* similar to that seen on th great toe when there is impairment of peripheral circulat on While *a terosclerotic ulcers* (p 1763) are more frequent in older pat ents than *is generally recognized* the ast majority of peptic ulcer pati nts show no evidence of systemic or local *atherosclerosis* Pept c ulcer has occurred in the course of *periarteritis nodosa* (p 10°) of great clin cal *severity* but th s *observation* is not of general importance

Toxemia —Toxemia produces ulceration of the *stomach* and duodenum This mechanism is operati e in lesions that occur after severe *burns* or *freezing after an upper respir tory i fection* or a *pneumon a* Nevertheless this cannot be the usual mechanism nor the whole *story* of the pathogenesis of the disturbance That tox c and pharmacologic factors are potential contributing causes is suggested by the *regular production* by *cinchophen* of duodenal ulcers in dogs and by the not infrequent occurrence of ulcer in humans with *acute* yellow atrophy

Alcohol and Tobacco —There is considerable d fference of opinion concerning the relationship of alcohol and tobacco to peptic ulcer Certainly *an acute* exacerbat on *of* ulcer symptoms may be provoked by overindulg nce in alcoholic beverages During the *course of* an exacerbation very sufferer from ulcer knows that the drinking of liquor produces discomfort Nevertheless in the periods of remission t is possible to drink moderately with mpunity Most observers agree that *al ohol may be an exciting fa tor* in the production of an exace bat on but certa nly plays no fundamental role in the pathogenesis

It is much more difficult to assign the role of *t bacco* Ther are many who believe that tl e *trophic changes* in the mucosa result from the effect of n cot ne and like substances upon tl e componer ts of the involuntary nervous system Ma y patients note that they suffer an increase in symptoms when they smoke In this respect the p pe and cigar *seem more noxious* than cigarettes Other patients smoke with impunity and may even report a certain amel ora t on *of distress wl en they puff* on a cigarette During intervals of rem sion there is l ttle d ubt but that their smoking caus s no damage

As with alcohol it is unlikely that smoking plays an important fundamental role in the production of peptic ulcer It is *possible that* in a small number of highly susceptible individuals such a mechanism may be operative If this were universally true peptic ulcer would be much more commonly encountered and would be more frequent in women

Food—The relationship of food to peptic ulcer is another unsettled point Most patients attribute the onset of an exacerbation to some dietary indiscretion such as the ingestion of spiced foods or of an excessive amount of food Despite this the relative unimportance of the diet is attested by the observation that during the active phase of the disturbance the ingestion of sterile distilled water may produce distress whereas in the free periods the most indigestible foods are taken with relative comfort and considerable zest

Factors That *Prevent Healing*—The continued operation of predisposing and excitin factors must tend to prevent healing of the ulcer Probably the most important single element is the continual bathing of the lesion with *hydrochloric acid* and *pepsin* The rationale for *gastro enterostomy* (p 1758) is based upon drainage of the gastric secretion in order to protect the ulcer and permit it to heal The unfortunate circumstance about this procedure is the fact that in a *fair proportion of* instances th healing of the gastroduodenal ulcer is effected at the price of a *marginal ulcer*

The main accomplishment of the local measures used in the treatment of peptic ulcer ncluding the prescription of *diet antacids* and protectives is essentially to combat the perpetuating influences of gastric secretion So far as the fundamental disturbance is concerned this type of regimen *compares to topical* application used for a trophic ulcer of the toe it



Fig 396—Ga tric ulcer in section showing interruption of musculature and extensive scar formation

does not strike at the fundamental difficulty and affords little promise of permanent or complete relief

Summary—The *following is* a p rsonal expression which summarizes the present state of our information relative to the etiology and pathogenesis of ulcer

Patients of a certain anthropomorphic and vegetative pattern under emotional stress tend to develop the individual reaction picture of a peptic ulcer The lesion is probably produced through the direct mechanism of acid digestion When produced failure of the ulcer to heal is probably dependent upon chemical factors particularly the constant bathin of the lesion with hydrochloric acid and pepsin The therapeuti program is aimed at the management of the basic distant disturbance and the control or eradication of exciting fa tors

Pathology—*Peptic* ulcer of the duodenum stomach or esophagus represents a physical defect in the mucous membrane *It may* vary in size from pinhead to the diameter of a silver dollar Smaller ulcerations are usually acute or represent the healing phase of a chron lesion They may extend into the wall of the stomach or duodenum or actually perforate into the free peritoneal cavity or into any of the adjacent viscera

Gastric ulcerations have a tendency to locate on the lesser curvature or on the adjacent anterior or posterior walls they more frequently are seen toward the distal end of the lesser curvature *Duodenal ulcers* may be single or multiple in the latter variety there is the special type of kissing ulceration in which two ulcers face each other on opposite sides of the lesser curvature

• MacCallum Textbook of Pathology

The Base and Edges—The lesions present a base composed of granulation tissue At the proximal border there is an overhanging rim of gastric mucosa the lower edge toward the pylorus does not have this conformation Thrombosed arteries and veins are not infrequently seen in the base of ulcerations

Healing—The gastric type of ulcer usually heals in such fashion that it is difficult to find any evidence of a previous lesion other than a small mucosal scar In the duodenum the healing process usually results in the formation of a good deal of scar tissue As a result, the lumen of the first or occasionally of the second portion of the duodenum may be deformed and even narrowed in caliber If this narrowing is only moderate it may not give rise to any clinical manifestation However if it is severe or if there are recurrences of the ulceration with increase in scar tissue formation a dense fibrous stricture sufficiently narrow to prevent the egress of food is produced Under such circumstances there is a compensatory enlargement in the capacity of the stomach Hypertrophy of the musculature occurs if the compensatory mechanisms are adequate to overcome the narrowing Where such do not exist there develops a balloon like stomach with an extremely thin wall, showing feeble peristalsis

Complications—The complications of peptic ulcer include gastritis hemorrhage penetration perforation malignancy and obstruction

GASTRITIS—In association with actual ulceration the remaining mucosa does not maintain a normal appearance Almost invariably there are varying degrees of *acute or chronic gastritis* (p 1808) The latter not infrequently is of the cobblestone hypertrophic type

HEMORRHAGE—As ulcers increase in depth they gradually encroach upon large blood vessels and may erode an artery or vein with resultant hemorrhage Should an artery be involved a rapidly lethal outcome is a possibility but venous involvement is less ominous

PENETRATION AND PERFORATION—With increase in depth the ulcer may involve the serosal surface of stomach or duodenum As a result a *perforation* into the free *peritoneal* cavity may occur If the process occurs sufficiently slowly there may be opportunity for walling off with the formation of a penetration and intraperitoneal abscess

MALIGNANCY—In our experience gastric ulcers rarely become malignant we have never seen carcinomatous degeneration of a duodenal ulceration There is a negative correlation between duodenal ulceration and carcinoma of the stomach in that the latter is very rarely seen in association with the former

OBSTRUCTION—A late complication of healed peptic ulcer is intense scarring with *hour glass deformity* of the stomach or a *pyloric stenosis* One of the astounding observations of clinical practice is the degree of obstruction that can exist in the presence of normal health

Clinical Manifestations—The peptic ulcer may be asymptomatic or productive of typical or atypical manifestations

Asymptomatic Ulcer—Asymptomatic ulcer must occur quite commonly evidence of this is furnished by the frequent observation at necropsy of healed ulcers in cases in which the histories gave no evidence of the clinical presence of the lesion This remarkable tendency to heal is important prognostically

Characteristic Syndrome—In its usual form the symptoms of peptic ulcer are characterized by the site of pain its time relationship relief from ingestion of food and recurrent epochs of distress alternating with period of remission

The characteristic distress is frequently described as a sensation of hunger aggravated to the point of being painful it may vary from a mild sense of epigastric discomfort to agonizing piercing pain and it is usually *sharply localized* to the epigastrium With penetration of the lesion pain radiates through to the lower thoracic spine the subcostal margin on either side or the left shoulder

The typical ulcer pain occurs *within two to three hours after ingestion of food* and tends to waken the patient especially in the early morning hours Less often the pain comes on during meals in ulceration of the

second portion of the duodenum it may be immediately postprandial with ulcers of the lesser curvature it occurs one or more hours after the meal

The typical ulcer pain is relieved by ingestion of food antacids sedatives and protectives (p 1750)

Ulcer pain is characterized by its regularity of occurrence It comes on three or four times daily at regular intervals following meals, it awakens the sufferer with the inexorability of a time clock at some given hour in the early morning The pattern of discomfort is repeated daily for several days, weeks or months The active period is followed by a phase of remission which may last for days, weeks months years or even decades

It is because of the periods of *remission* in peptic ulcer that so many therapeutic claims have been made for so wide a variety of procedures A similar explanation underlies the difficulty of evaluating the efficacy of any therapeutic measure since the patient in a phase of remission may be able to eat any type of food or beverage with impunity

Atypical Symptoms—The typical features of peptic ulcer may be conspicuously absent Individuals who are hyposensitive to pain may have as herald symptoms only *bulimia* or *nocturnal hunger* Patients who substitute hunger for pain prevent discomfort by eating frequently they avoid nocturnal misery by ransacking the icebox at bedtime These pain substitutes may be the only subjective manifestations despite definite radiographic evidences of ulceration

On rare occasions the first symptom of a peptic ulcer is a *sudden hemorrhage* due to erosion of large sized vessel Again the first inkling of ulceration may be the manifestations of an acute abdominal catastrophe due to *penetration* or *perforation* This type of onset occasionally follows or accompanies an acute alcoholic bout under which circumstances the diagnosis is clouded by other manifestations of the indiscretion

The Diagnosis of Peptic Ulcer—The diagnosis of uncomplicated peptic ulcer rests almost entirely on the history *Physical examination* at best reveals an area of epigastric tenderness Analyses of *stomach contents* and *stool* afford little definitive information *hydrochloric acid* is usually present in increased or at least normal amounts but the type of acid curve may vary in any given direction the *stool* does not give a positive test for occult blood in uncomplicated ulcer

Confirmation of the diagnosis of uncomplicated peptic ulcer requires gastro intestinal *radiographic examination* Incontrovertible radiographic evidence of ulcer is the presence of a *niche* indirect presumptive evidence is afforded by deformity or irregularity particularly in the region of the duodenal cap The ulcer may be visualized by *gastroscopy* but it is only in a rare instance that this type of examination is justifiable A characteristic ulcer curve may be obtained by *electrogastrography*

The ulcer that is *complicated* by bleeding or obstruction offers less of a diagnostic problem *Blood* may be recognized in vomitus and with moderate to severe hemorrhage the characteristic *tarry stool* is passed with constant ooze and a *persistent positive test* for *occult blood* in the feces (p 3728) a suspicion of malignancy is entertained

Differential Diagnosis—Peptic ulcer is to be differentiated from a *func*

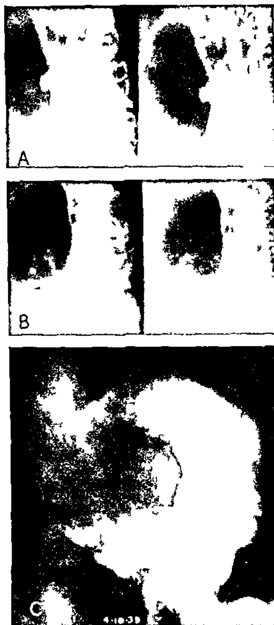


Fig 397 —*A* Typic l small knob-like ben gn ulcer niche projecting f om the less curvatur on serialgrams taken in extreme obl que pos t on w th comp ess on on Ma ch 10 1939 The e was no ind cation of edema or infiltrat on at the ulcer base *B* On April 1 1939 the niche was gone but th e was a su gestion of sl ght distortion of the mucosal rel ef t the te of the pr viou crate *C* On April 10 the less r curvature appe red normal

second portion of the duodenum it may be immediately postprandial with ulcers of the lesser curvature it occurs one or more hours after the meal

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can be no doubt concerning the benign nature of the lesion but *with gastric ulcer there may be considerable difficulty* The presence of *free hydrochloric acid* in the stomach content points away from a malignancy yet *even this is not incontrovertible evidence of a simple peptic ulcer* *Persistent bleeding failure to respond to treatment low or absent acid and the palpation of a mass suggest malignancy* though a delay occasioned by awaiting these positive findings may forfeit the possibility of surgical excision

Malignancy is more likely to occur in individuals over the age of forty particularly if there has not been any previous attack in earlier life With marked anorexia loss of weight and strength and a secondary anemia the presence of cancer is strongly suspected Knowledge of the location of the lesion is of considerable assistance Duodenal ulcers are always benign erosions along the greater curvature of the stomach are almost invariably

TABLE 121—DIFFERENTIAL *DIAGNOSIS* OF GASTRODUODENAL LESIONS

	Gastric Neurosis	Peptic Ulcer	Gastric Malignancy
Age	*Usually below 40*	*Usually below 40*	Usually *over 40*
Sex	Either	Usually male	Usually male
Hydrochloric acid	Variable	Usually increased	Decreased or absent
Histamine achylia	*No*	No	*Yes*
Blood in gastric contents	No	No	Yes
Occult blood in stool	No	No	Yes
Appetite	Variable	Increased	Decreased
Roentgen findings	No organic defect	*Duodenal* or gastric deformity	Gastric deformity
Response to treatment	Good	Good	Usually poor

malignant ulcers located in the prepyloric region between incisura angularis and pylorus are malignant in more than 60 per cent of instances The *size of an ulcer* is of no aid a small lesion may be malignant whereas a large one may be benign When it is available gastroscopy may be most helpful Symptomatic relief following *conservative* therapy is not proof that malignancy does not exist

In instances of doubt *the clinician owes it to the patient and himself* to demand an *exploratory procedure* but even with the abdomen opened the surgeon may be uncertain Inflammatory glands in the *region* of the pylorus may give the impression of a metastatic deposit but it is not until the tissue is sectioned that a positive statement can be made The most astute surgeon knows that both pleasant *surprises* and bitter disappointments are in store following histological examination

An onset *with* perforation particularly in an alcoholic may simulate the

tional neurosis on the one hand and, on the ominous side from a gastric malignancy

Gastric Neuroses—The clinical picture of *peptic ulcer* and that of hypersthenic gastric neurosis may be identical Differentiation between the two conditions requires diagnostic roentgenography with positive dem

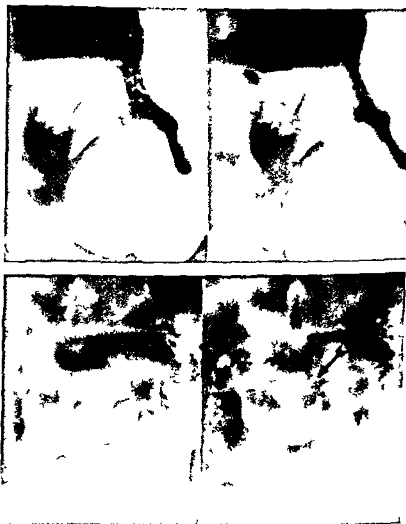


Fig 398—Serialgrams of a patient with duodenal ulcer to illustrate the value of compression The upper two exposures without compression show no evidence of ulcer or irritability In the lower two exposures with compression a relatively large ulcer fleck is clearly demonstrated *

onstration of organic deformity In duodenal ulceration radiographic evidence should be obtained almost without exception but gastric ulcers are much less easily shown

Gastric Malignancy—The most important diagnostic problem in suspected ulcer is the exclusion of malignancy *With a duodenal lesion* there

* Bockus Gastro-enterology Vol I

Hepatobiliary	Cholelithiasis and cholecystitis Look for radiopaque shadows and perform cholecystography (p 2000) Acute yellow atrophy of liver with jaundice and diminution in size of liver Biliary cirrhosis with splenomegaly fever and clubbed fingers

symptoms of *acute gastritis* positive evidence of perforation is obtainable from the roentgenologic demonstration of free air under the leaf of the diaphragm or through the contents obtained by abdominal puncture (p 1893) With negative evidence there may be still justifiable doubt that can only be satisfied by an exploratory laparotomy

The Course of Events in Peptic Ulcer—The course of events in peptic ulcer varies There may be (*1*) complete relief of symptoms and healing (*2*) a wave like sequence with phases of remission and exacerbation (*3*) a change in the clinical picture resulting from complications such as perforation penetration obstruction hemorrhage and malignancy

Spontaneous Healing—From the evidence obtained by radiographs and at autopsy spontaneous healing must occur in a large majority of instances and this fact favorably influences the prognosis

Wave like Course—The course of peptic ulcer often is wave like being punctuated by periods of *exacerbation* and *remission* These episodes may be characterized by a definitive pattern symptoms may appear in the spring and fall with the same periodicity as the seasons

Complications—The cyclic course may go on for years or even decades without any appreciable change in the symptoms but more often repeated episodes become modified by the appearance of complications

Functional or Organic Pyloric Obstruction—Pyloric obstruction may be organic or functional During the clinical course of a duodenal ulcer at a time when there is a considerable inflammatory reaction in the surrounding mucous membrane and musculature a state of prolonged spasm in the duodenal circular muscles frequently results in *functional pyloric obstruction* This process prevents the relaxation necessary to receive the gastric contents reverse peristalsis is inaugurated and nausea develops The patient suffers bouts of persistent vomiting which lead to *hypochloremia* (p 732) the losses of water sodium chloride and hydrochloric acid result in *alkalosis* (p 722) associated with elevation of the carbon dioxide combining power of the blood The patient loses weight becomes dehydrated and may develop *tetany* (p 723) failure to ingest food or fluid produces severe constipation oliguria and even anuria Though urinary symptoms are not usually accompanied by demonstrable organic change in the kidney anatomic evidences of a severe *nephrosis* (p 2389) with calcification of the convoluted tubules may be found

The *organic type of pyloric obstruction* follows several ulcer cycles and is the result of cicatrization in the first or second portions of the duodenum The clinical symptoms are similar to those of functional obstruction except that marked dilatation of the stomach may be demonstrable in radiographs

Hemorrhage—In peptic ulcer bleedings are usually acute rather than insidious The hemorrhage may or may not cause systemic reaction If

DIFFERENTIAL DIAGNOSIS OF

Epigastric Pain

Pain in the pit of the stomach is frequently encountered The diagnostic problems involved are of paramount importance from the standpoint of surgical indications and contraindications Failure to recognize the herald symptoms of an appendicitis may lead to grievous delay for example laparotomy performed in the presence of an acute coronary occlusion may prove fatal

	DIAGNOSTIC FEATURES
Parietes	
Epigastric Hernia	With sharply localized midline pain and tenderness and demonstrable sac (p 1799)
Neurogenic	
Gastric Crisis	*In tabes dorsalis with pupillary* and reflex changes Pathognomonic findings in the cerebrospinal fluid (p 3734)
Metabolic	Insulin shock or diabetic acidosis History of injection and urinary *findings*
Circulatory	
Angina Pectoris	With relief from nitroglycerin (p 890)
Coronary Occlusion	Acute indigestion often with fever and leukocytosis simulating an acute infection Definitive diagnosis from Ecg (p 983) Later development of pericardial friction rub
Fibrinous Pericarditis	*With characteristic to and fro shuffle* (p 1007)
Digestive	
Hygienic Error	Gluttony Ingestion of irritant foods or drinks Alcoholism
Acute Gastric Dilatation	With copious returns by gastric intubation (p 1807)
Gastric Neuroses	*Of hypersthenic or hyposthenic* varieties Gastric analyses reveal hyperacidity hypoacidity or hypersecretion X rays show only spasms or ptosis
Gastritis	*Acute or chronic X ray shows rugal* changes (p 1808) Proven only by gastroscopy
Cascade Stomach	Congenital anomaly recognized only by x ray (p 1805)
Peptic Ulcer	Hunger pain Free acid in gastric contents Gastroduodenal deformity in barium meal (p 1786)
Gastric Malignancy	With anacidity and persistent positive stool examinations for blood (p 1814) Filling defects in barium meal (p 1817)
Duodenal	Ulcer or duodenal ileus recognized by x ray (p 1804)
Cancer of Transverse Colon	With persistent positive findings for blood in the stool (p 3721) Filling defects in barium meal and barium enema (p 1888)
Hemorrhagic Pancreatitis	*With acute pain accompanied by shock* (p 1933) *Demonstrable areas of fat necrosis* at laparotomy (p 1940)
Acute Appendicitis	As herald manifestation before localization of *discomfort to right lower quadrant*

CONTINUED

conservative treatment (2) a small percentage additionally require bed rest (3) hemorrhage is an acute medical emergency (4) perforation re quires immediate surgical intervention (5) interval surgery is reserved for the treatment of complications and the management of ulcerations that have features leading to the suspicion of malignancy

Psychotherapy—The patient with peptic ulcer should be familiarized with the *natural course* of his disability He must be warned of the peril of *exacerbation* on provocation and reassured concerning the extraor dinary tendency of the ulcer to heal if given an opportunity he must be aware of the varieties of complications so that early signs such as tarry stool are recognized but he must also be assured that only a small num ber of ulcer patients develop unhappy sequels

The patient is urged to describe his way of life (p 3473) in order to bring out possible exciting circumstances such as long hours of work pro longed strain excessive use of alcohol or tobacco injudicious diet faulty eating habits particularly of mastication

When tangible exciting circumstances have been enumerated inquiry is made into surface *emotional disturbances* such as business strain fam ily difficulties maladjustments in the home or in social or business inter course worries and doubts concerning the health and welfare of the fam ily group and frustration in business school home or love life Only in rare instances does the peptic ulcer patient require reference to the trained psychotherapist

Sippy Treatment—Conventionally the patient is placed on the *Sippy regimen* (p 666) Patients with severe ulcer pain begin their cure with whole milk or a mixture of milk and cream in the proportions of 1 to 3 given in 2 ounce quantities every two hours during the day and at four hour intervals at night the night doses may be increased later to 4 to 6 ounces

Since this diet is unbalanced and deficient it should be discontinued as soon as severe symptoms have abated Thereafter the progressive Sippy regimen (p 666) is instituted

Patients who have not severe discomfort are started on the first or second week Sippy diet (p 666) with a rapid increase as the symptoms abate in the variety and quantity of food

The medicinal adjuvants consist of *Sippy powders* (p 1754) employing the magnesium powder (p 1755) in the presence of constipation and cal cium (p 1755) if there is diarrhea A mild sedative such as sodium pheno barbital in 16 mg (¼ grain) doses before each principal meal is advisable and a belladonna preparation is prescribed if the manifestations are vago tonic with spasmosis and bradycardia

Author s Routine—The senior author does not ultilize the Sippy rou tine The diet is unbalanced many patients object to milk and become cloyed with the monotony of their feedings the powders favor an alkalosis which if continued may lead to kidney damage calculus formation alka losis and tetany

It is our custom to inquire into the dietary habits of the patient and arrange a bland diet consisting of three principal meals and three inter mediate feedings The *breakfast* may include either cooked cereal or eggs and tea and toast for *luncheon* and *dinner* there is a principal course of

it is sufficiently great there are the usual phenomena of exsanguination and shock if it is milder it may result only in transitory weakness or faintness and melena Regurgitation of blood from duodenum into stomach may cause nausea followed by hematemesis (p 1764)

Perforation—Perforation is fortunately a rather infrequent complication of peptic ulcer As with hemorrhage it may in rare instances be a herald clinical manifestation Duodenal and juxtapyloric ulcerations are most prone to perforate freely

Perforation of the ulcer causes acute *shock* agonizing *abdominal pain rigidity tenderness* and *loss of liver dullness* In about 80 per cent of cases free air is demonstrable radiographically under the diaphragm



Fig 399—Air under both diaphragms Perforation of duodenal ulcer

Malignancy—Malignant degeneration of a gastric ulcer is stated to occur in 2 per cent of patients Advocates of the theory of malignant degeneration regard this figure as low, others including the authors believe that peptic ulcer rarely becomes malignant and that such examples as are encountered represent an initial malignancy with secondary ulceration With the slightest suspicion of malignancy surgical intervention should not be delayed It is far safer to perform scores of unnecessary procedures and obtain definitive assurance of the benign character of a lesion than to procrastinate once at the cost of operability

With duodenal ulcer we have never seen malignant degeneration

The Treatment of Peptic Ulcer

The treatment of peptic ulcer is governed by several fundamental principles (*1*) The vast majority of uncomplicated ulcers yield to ambulatory

* Buckstein Clinical Roentgenology of the Alimentary Tract

have been reduced to four a day an attempt is made to stop the midday and/or morning doses of black medicine but evening and bedtime doses of Mistura Nigra are continued for a prolonged period of time

Conservative Bed Treatment—Patients who fail to respond to the ambulatory routine at the end of a week or ten days are ordered to bed Sometimes a *week end rest* (p 3754) will suffice Patients who cannot afford to leave work may take a *partial rest cure* (p 3754) by going to bed immediately after the day s work is done and remaining in bed until it is time to leave again in the morning This is easier for the laborer than the housewife whose working hours are not regulated

When possible bed rest should be complete results are more satisfactory if the patient is *institutionalized* (p 3754) The same diet and medications are employed as in ambulatory treatment Heat is applied to the abdomen after each principal feeding and preferably after the intermediate feedings as well If the patient does not think that this regimen is sufficiently elaborate to warrant bed rest *packs* (p 3790) are substituted for the simpler and equally effective electric pad

The Milk Drip—With severe intractable pain which does not respond to the ordinary dietary means the use of a milk drip has been suggested for the continuous neutralization of gastric acidity By this method a tube is passed into the stomach and attached to a container which permits a graduated administration of whole milk at a rate which may be varied from 15 to 30 drops per minute The drip is continued day and night until pain is completely relieved Relief may take two or three days but rarely requires a longer time In order to prevent curdling of the milk in the stomach with resultant obstruction of the tube 10 cc of a 3 per cent solution of sodium citrate are added to each quart of milk In general 2000 cc daily of whole milk are sufficient to give complete relief of symptoms occasionally it may require as much as 3000 cc

Irritation from the indwelling tube frequently gives rise to a *traumatic pharyngitis* which may be manifest by the occurrence of a sore red throat and pain referred to the ear *decubitus ulcers of the esophagus* (p 1736) have been observed from pressure of the tube These manifestations may be prevented by the use of a latex tube inserted into the stomach with the aid of a stylet When the milk drip is discontinued the patient is placed on the Sippy diet (p 1791)

The drip may be carried out with milk substitutes such as aluminum hydroxide diluted with 3 parts of water and undiluted aluminum phosphate The latter requires the use of a special air valve to prevent clotting

The senior author himself a sufferer from peptic ulcer is particularly averse to these instrumental procedures It is his belief that intubation adds to patient discomfort there is no need for a drip during the waking hours when the patient can sip his milk Nocturnal symptoms are usually successfully controlled by a feeding at bedtime If pain awakens the victim he may sip warm milk from a conveniently placed thermos bottle and eat a few soda crackers he may prevent periodical and obstinate night pain by setting his alarm to ring shortly before the anticipated pain and taking the feeding before distress is noted

Parenteral Injections—Parenteral injections of various protein cleavage products have been popularized in the treatment of peptic ulcer The

eggs creamed chicken finely chopped hamburger steak or boiled fish mashed potatoes a vegetable puree and a simple dessert such as a pudding or a custard *Intermediate feedings are given in the middle of the* morning the middle of the afternoon and at bedtime They consist of crackers and milk crackers and cold cereal and freshly prepared or canned soup with rice or unsalted crackers Coffee is absolutely banned

Supplementary vitamin administration is advisable Before each principal meal and again at bedtime we prescribe belladonna drops and after each meal a teaspoonful of *Mistura Nigra* (p 1757) With each intermediary feeding and at bedtime an *antacid* is employed preferably of the physical group such as aluminum (p 1754) but when there is constipation milk of magnesia in fluid form or tablets is substituted A *hypnotic* is given with the bedtime dose of belladonna If an electric pad is available the patient

TABLE 192 —ULCER TIME TABLE

7 to 8 A M	Belladonna drops novatropine 2 mg or syntropan 50 mg vitamin Breakfast Mistura Nigra
10 to 11 A M	Antacid aluminum or magnesia Midmorning feeding
Noon	Belladonna or substitutes Luncheon Mistura Nigra
3 P M	Antacid Mid afternoon feeding
6 to 7 P M	Belladonna or substitute Supper Mistura Nigra
10 to 11 P M	Belladonna or substitute hypnotic Bedtime feeding Antacid
12 M–6 A M	For night pain the alarm clock is set for half hour before the expected distress and the intermediate feeding and antacid are repeated

may sleep with the pad on the abdomen provided that the switch is on the lowest degree of heat

Gastric mucin in our experience is too unpalatable and unwieldy for routine use it is reserved for patients with obstinate symptoms The administration of *olive oil* is recommended in patients with marked hyperacidity clinical trials with enterogastrone (p 1821) indicate the potential utility of this intestinal hormone which inhibits gastric motility and reduces the secretion of HCL (hydrochloric acid) Intractable ulcers may respond to a *pepsin inactivator* For this purpose sodium alkyl sulfate 0 2 gm may be given every two hours followed in an hour by a milk and cream mixture

Rarely does the patient fail to respond to treatment As improvement occurs the mid morning feeding may be omitted and later the mid afternoon repast but the bedtime feeding is continued indefinitely When meals

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When possible bed rest should be complete results are more satisfactory if the patient is *institutionalized* (p 3754) The same diet and medications are employed as in ambulatory treatment Heat is applied to the abdomen after each principal feeding and preferably after the intermediate feedings as well If the patient does not think that this regimen is sufficiently elaborate to warrant bed rest *packs* (p 3790) are substituted for the simpler and equally effective electric pad

The Milk Drip—With severe intractable pain which does not respond to the ordinary dietary means the use of a milk drip has been suggested for the continuous neutralization of gastric acidity By this method a tube is passed into the stomach and attached to a container which permits a graduated administration of whole milk at a rate which may be varied from 15 to 30 drops per minute The drip is continued day and night until pain is completely relieved Relief may take two or three days but rarely requires a longer time In order to prevent curdling of the milk in the stomach with resultant obstruction of the tube 10 cc of a 3 per cent solution of sodium citrate are added to each quart of milk In general 2000 cc daily of whole milk are sufficient to give complete relief of symptoms occasionally it may require as much as 3000 cc

Irritation from the indwelling tube frequently gives rise to a *traumatic pharyngitis* which may be manifest by the occurrence of a sore red throat and pain referred to the ear *decubitus ulcers of the esophagus* (p 1736) have been observed from pressure of the tube These manifestations may be prevented by the use of a latex tube inserted into the stomach with the aid of a stylet When the milk drip is discontinued the patient is placed on the Sippy diet (p 1791)

The drip may be carried out with milk substitutes such as aluminum hydroxide diluted with 3 parts of water and undiluted aluminum phosphate The latter requires the use of a special air valve to prevent clotting

The senior author himself a sufferer from peptic ulcer is particularly averse to these instrumental procedures It is his belief that intubation adds to patient discomfort there is no need for a drip during the waking hours when the patient can sip his milk Nocturnal symptoms are usually successfully controlled by a feeding at bedtime If pain awakens the victim he may sip warm milk from a conveniently placed thermos bottle and eat a few soda crackers he may prevent periodical and obstinate night pain by setting his alarm to ring shortly before the anticipated pain and taking the feeding before distress is noted

Parenteral Injections—Parenteral injections of various protein cleavage products have been popularized in the treatment of peptic ulcer The

suggested remedies include casein typhoid vaccine, larostidin (5 per cent histidine) synodal (emetine), and activin In our opinion this form of treatment is irrational the results obtained may be credited to the spontaneous healing of the ulcer or the powers of persuasion of the injector

Medical Management of Bleeding Peptic Ulcer—The *surgical indications* in the presence of bleeding peptic ulcer are discussed later (p 1796) When bleeding is derived from an artery it is usually so rapidly exsanguinating that there is no opportunity for medical treatment Fortunately in the great majority of patients bleeding from the peptic ulcer is venous in origin Patients are preferentially treated by medical means during the acute stage of the hemorrhage Attempts at radical surgery during active bleeding result in a high operative mortality

In conservative management the patient with a bleeding peptic ulcer is put to bed and covered with warm blankets Hot water bags are placed at the feet the foot of the bed is elevated about 12 inches and the patient s face is turned to one side or the other at frequent intervals Opiates are given in repeated dosage until restlessness is controlled dilaudid 2 mg ($\frac{1}{32}$ grain) is preferred because of its lesser tendency to produce emesis

The use of infusions and transfusions during active bleeding is disputed Opponents argue that the drop in blood pressure resulting from severe hemorrhage serves the useful purpose of diminishing the amount of blood loss and hence efforts that might elevate blood pressure oppose the means utilized by nature to stop bleeding They agree that when blood pressure falls to a level at which life is endangered transfusion is mandatory We who are proponents of transfusion by the drip method favor replacement of lost blood The slow infusion does not elevate blood pressure sufficiently to perpetuate hemorrhage and prompter treatment is wholly salutary

Differences of opinion exist relative to feeding in bleeding ulcer There are those who advocate starvation until there is clinical evidence that bleeding has ceased We advocate feeding from the very day of a hemorrhage Usually the discussion is best settled by the patient If he is vomiting feeding is obviously unwise On the other hand if there is appetite and a demand for food it is wise to quiet the stomach with what appeals to the palate of the sufferer The best known dietary regimen is that advocated by Meulengracht (p 667) However if the patient is unable to tolerate the types of food administered in this diet the Sippy regimen may be started

Surgical Treatment—In our opinion the surgery of uncomplicated peptic ulcer is unwise and unwarranted unless in gastric lesions there is a suspicion of malignancy Surgical treatment (p 1758) for peptic ulceration is concerned with such complications as perforation obstruction hemorrhage and the fear or actual presence of a malignant process

Surgical Treatment of Perforation—The occurrence of a perforation is an *absolute surgical indication gastrorrhaphy* (p 1758) is the simplest procedure but some surgeons perform a *subtotal gastrectomy* (p 1759) arguing that individuals who develop a perforation are prone to have frequent exacerbation of ulcer symptoms or to develop pyloric obstruction

Surgical Treatment of Pyloric Obstruction—The presence of a pyloric

obstruction is a *relative indication* for surgery Since the great majority of obstructions are spastic in origin the patient should be given an opportunity of demonstrating how much of the obstruction can be relieved by purely medical means Under careful supervision the patient is put to bed and given sedatives Fluids and semisolids are given orally in small doses water loss and dehydration are corrected by the use of intravenous fluids and gastric lavage is performed before breakfast and about six hours after the last evening meal If the amount of gastric retention is decreasing conservative treatment is justified for at least two or three weeks At the end of this time if nocturnal retention remains as high as 400 to 500 cc and the patient is not gaining weight a surgical approach to the problem should be considered The preliminary treatment helps restore gastric tonus and aids in the prevention of postoperative complications

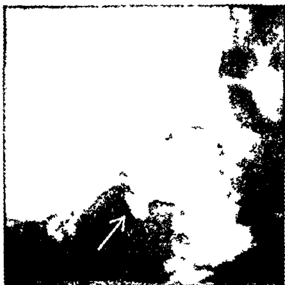


Fig 400—Niche of a jejunal ulcer with shortening of contour at site of n[illegible]

The operative procedure to be employed is still a matter of serious discussion Most surgeons prefer a *posterior short loop gastro enterostomy* (p 1759) an operation that has the advantage of technical simplicity However gastro enterostomy is followed by recurrence of ulceration in approximately 30 per cent and jejunal ulcerations are often the most difficult to treat In consequence the recent trend has been to perform *subtotal gastrectomy* (p 1759) as the procedure of choice With subtotal gastrectomy the primary mortality rate varies between 1 and 10 per cent Jejunal ulceration following subtotal gastrectomy is relatively infrequent but much more difficult to handle than that occurring following gastro enterostomy

For an individual with organic pyloric obstruction who is otherwise in good health and whose gastric musculature has good tone we advocate subtotal gastrectomy by an experienced surgeon When optimum condi

tions are not present, it is probably wiser to perform gastro enterostomy with its lesser immediate risk

Of Hemorrhage—Recurrent severe hemorrhage requires consideration of a subtotal gastrectomy (p 1759) to remove the ulcer and eliminate a complication which in itself may be fatal In the approach to this decision the conservative practitioner recalls that a fatal outcome from hemorrhage in a patient under forty years of age is rare and hemorrhage in women infrequently terminates life However in an individual who has reached the age of forty five or over and who has had repeated hemorrhages we advocate surgery since it is in this group that the greatest percentage of fatalities occur Gastro enterostomy does not offer a cure for the bleeding ulcer and the more radical procedure is clearly advised

Intractable Symptoms—Intractable ulcer symptoms with frequent recurrences are usually found in individuals of unstable personality and those who have insoluble psychogenic problems Bilateral supra or infra-diaphragmatic vagotomy (p 1760) may prove palliative to these patients precluding the necessity for mutilating procedures involving the stomach itself Following vagotomy gastric emptying may be delayed to the point where gastro-enterostomy is required Successful vagotomy is associated with freedom from pain and abolition of gastric secretion following a sham meal or injections of insulin

Suspicion of Malignancy—The suspicion of malignancy is a definite indication for radical surgery Since serial histological sections may be required to solve the problem nothing short of subtotal gastrectomy is advised

CHAPTER 90

CLINICAL DISTURBANCES OF THE STOMACH AND DUODENUM LOCAL LESIONS WITH OR WITHOUT SYSTEMIC MANIFESTATIONS

CONGENITAL HYPERTROPHIC PYLORIC STENOSIS

The commonest congenital abnormality of the stomach of clinical importance is the hypertrophic pyloric stenosis

Clinical Manifestations—Clinical manifestations of hypertrophic stenosis appear about two months after birth and consist of explosive attacks of projectile vomiting shortly after nursing The failure of sufficient nutriment to enter the intestines results in marked constipation oliguria and evidences of malnutrition The infant fails to gain weight and appears dehydrated

At the onset of symptoms the diagnosis is made before obvious physical signs develop through radiography which reveals enlargement of the stomach and retention of the gastric meal In more advanced instances physical examination gives incontrovertible evidence of the abnormality peristalsis is seen in the epigastrium the hypertrophic pylorus is palpable as a hard movable mass beneath the right costal border or in the epigastrium (p 1814)

Treatment—Conservative treatment consists of frequent small feedings and physiologic doses of antispasmodics Atropine sulfate 1 5000 solution

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A



B

Fig 401 —Congenital pyloric stenosis *A* Appearance after filling stomach with barium *B* Appearance six hours later

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is added to the formula in increasing amounts until a clinical effect is observed *drug therapy is interrupted* when evidences of belladonna sensitivity or poisoning (p 3816) such as mydriasis erythema restlessness convulsions and fever are encountered The feeding of *thick cereals* that cannot be expelled during emesis is sometimes successfully practiced in less severe examples fluid requirements are met by small *rectal infusions* or *hypodermoclyses* (p 3771)

Surgery—With increasing weight loss and failure of conservative treatment *surgical intervention* is indicated The procedure of choice is the *Rammstedt operation* which is essentially a pylorotomy in which the hypertrophic muscles are incised down to the mucosa (p 1759) The results of surgery are brilliant the risk is comparatively slight considering the poor nutrition of the patient and the urgency of the symptoms

Postoperative Care—Following operation thick cereals and frequent feedings are resumed The child often gains considerable weight within a short time and may proceed to develop without further disturbance In the immediate preoperative and postoperative periods fluid and nutritional requirements are supplied by the institution of a continuous intravenous drip If there are no accessible veins in the extremities the jugular or the superior longitudinal sinuses are utilized for venipuncture

HERNIA

A hernia is a defect in the fascial wall of any of the body cavities Through the *sac* that is formed by the defect the normal contents of the cavity may protrude The *surgically important hernias are those of the* abdominal cavity and the common sites are (*1*) inguinal (*2*) incision lines of previous operative procedures (*3*) umbilical (*4*) epigastric (*5*) femoral (*6*) para esophageal hiatus of the diaphragm

The Types of Hernia—Inguinal hernias are of the indirect and direct varieties The *indirect inguinal hernia* results from a primary defect at the internal inguinal ring Through this a portion of the abdominal contents protrudes into the inguinal canal thence through the external inguinal ring and into scrotum These hernias are most common in young individuals and are most often due to congenital failure of closure of the processus vaginalis at the internal inguinal ring The clinical deformity may not appear until later in life or the congenital defect may be small and not become apparent until the intestinal content gradually dilates the original gap

Direct inguinal hernias protrude through a weak point in transversalis fascia mesially to the epigastric vessels and directly beneath the external inguinal ring Such hernias appear most often in elderly individuals and present a diffuse bulge which does not as a rule descend into the scrotum

Incisional hernias protrude through a weakness or defect in the scar of a previous abdominal incision They may involve a small portion of the scar or its entire length

Umbilical hernias are most often observed in infants and women The primary defect is an incomplete closure of the umbilical ring

Epigastric hernias occur in the median line just below the xiphoid process When irreducible they may produce symptoms suggesting peptic ulcer or coronary closure

Femoral hernias are also seen most often in the female The hernial protrusion takes place through the fat pad which lies medial to femoral veins The hernia extends along the vessels to the subcutaneous tissues of the upper thigh just beneath the inguinal ligaments

Irreducible Incarcerated and Strangulated Hernias—The contents of most hernias are easily replaced in the abdominal wall when the patient is recumbent Such hernias are called *reducible* Occasionally the content is not replaceable in the abdominal wall due to a very narrow neck or adhesions between the content and the sac If such content consists of bowel and the restriction to reduction is of sufficient degree to cause interference with the intestinal stream there is *partial or complete intestinal obstruction* and the hernia is *incarcerated* Here to the symptoms of the hernia are added the symptoms of intestinal obstruction (p 1873) and to the risk of herniorrhaphy is added the risk of treatment of the intestinal obstruction

When an incarcerated hernia exists gentle preoperative attempts are made towards its reduction The patient is placed in bed with knees elevated to relax the abdominal wall Then with gentle pressure an attempt is made to replace the hernial content Immersion of the patient in a warm bath sometimes gives increased relaxation of the abdominal wall permitting the reduction of hernias not otherwise reducible The administration of spinal anesthesia with the consequent marked relaxation of the abdominal wall also may permit many hernias to be reduced

If the above mentioned measures fail operation must be undertaken as an emergency procedure Technically the procedure differs from simple herniorrhaphy in that the neck of the sac must usually be incised to increase its size sufficiently to permit the reduction of the hernial contents

Hernias are considered *strangulated* when in addition to the incarceration there is sufficient constriction of the bowel to produce interference with the blood supply of the hernial content The incarcerated content may be either omentum or intestine Most incarcerated hernias if untreated for any length of time result in strangulation of the content and neglected strangulated hernias lead to infarction of the content and perforation of bowel

Strangulated hernias differ from incarcerated hernias in that the hernia itself becomes quite tender signs of intestinal obstruction are more severe the patient may be febrile and in shock Operation must be undertaken as an emergency procedure The risk of operation is marked averaging from 10 to 20 per cent If bowel or omentum has become infarcted the involved segment must be excised The technic of this procedure is the same as that of excision of a segment of bowel for tumor (p 1835) In such exigencies not only is the risk to life considerable but the probability of cure of the hernia by operation is markedly decreased due to associated edema of the abdominal wall structures around the site of the hernia Pre- and post operative penicillin and streptomycin are mandatory

Routine preoperative care is all that is necessary before simple herniorrhaphy but in incarcerated or strangulated hernia dehydration and shock are treated before operation The postoperative complications of hernia in addition to those common to any operation are those of infection of the wound or peritoneal cavity in instances of strangulated hernias

Diagnosis —The diagnosis of the hernias involving the abdominal wall poses no great difficulty for the practitioner who conducts a careful physical examination The inguinal hernia in the male may escape notice if there is no obvious bulge Under these circumstances the patient is examined while standing erect The external ring is palpated by inserting the finger through the scrotum The patient is directed to cough in order to demonstrate the impulse that is transmitted through the sac The regions of the femoral canal and the internal ring are palpated directly while the patient coughs

Incarceration of gut becomes obvious when reduction cannot be accomplished To effect the latter the patient is placed on his back with knees elevated in order to relax the abdominal wall Gentle pressure is attempted over the hernial sac while the hip joint is passively put through its range of motion in order to find an optimal position favorable to the return of the bowel to the peritoneal cavity Should this procedure fail the patient is placed in a warm tub and the manipulation is gently repeated At times the marked relaxation produced by *spinal anesthesia* (p 3782) successfully reduces the incarceration that fails to yield to simpler forms of therapy

Strangulation of the hernia is suspected when the area becomes tender and there are associated signs of *intestinal obstruction* Sooner or later the patient becomes *febrile* and may develop *shock*

Treatment —The repair of the hernia (*herniorrhaphy*) is a procedure of slight risk so long as the disturbance is uncomplicated An incision is made down to the hernial sac followed by its *excision* and the *repair* of the defect in the peritoneum muscle and fascia Recurrence is rarely observed unless the patient is obese and the tissues are flabby

The presence of hernial complications increases the risk to life and decreases the possibility of successful repair The *incarcerated hernia* is made hazardous by the accompanying *intestinal obstruction* (p 1873) The patient is dehydrated and toxic and the technical procedure requires that the neck of the sac be incised in order to increase its size sufficiently to permit return of the gut to the cavity provided that the loop is viable

The *strangulated hernia* offers the greatest technical difficulty the highest risk and the least possibility of a successful repair without recurrence The patient is often gravely ill and the operation is undertaken as an emergency procedure If the bowel is infarcted and gangrenous a *resection* (p 1835) is required Contamination of the peritoneal cavity is almost unavoidable and gross soiling may result from perforation although the use of penicillin (p 106) and streptomycin (p 103) pre and post operatively has greatly decreased the morbidity and mortality of strangulated hernia The postoperative course may be stormy due to toxic or obstructive *ileus* (p 1851) and/or *peritonitis* (p 1923)

Constitutional Factors in Relation to Hernial Repair —Herniorrhaphy is generally less successful *in elderly patients* because of *senile atrophy* of the muscular and fascial structures as well as the slower rate of healing The procedure is difficult and usually less successful in the *obese* who should be placed on a reduction diet for a considerable period of time before the operative repair is attempted Incisional and umbilical hernias are particularly prone to recur in the corpulent

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the "stay at home and more to be feared in the patient whose occupation or diversion involves travel

Trusses and Supports—Inguinal and femoral hernias that occur in patients who cannot or will not undergo herniorrhaphy require support by means of the truss This requires accurate fitting by an experienced technician The physician instructs the patient to apply the truss while recumbent after assurance that the contents have been reduced The patient is then examined while standing erect and after coughing in order to be certain that the truss accomplishes its best purpose

Abdominal and incisional hernias may require temporary strapping or the use of an abdominal binder or support

Hiatus Hernia

The hiatus hernia may occur through the *para esophageal opening* in the diaphragm or in the region of the *ligament of Treitz* which binds the fourth portion of the duodenum to the posterior abdominal wall The herniated structures rarely are invested in a peritoneal sac

PARA ESOPHAGEAL HERNIA

Para esophageal hernia is not at all an uncommon condition It is due to a congenital or acquired weakness of the esophageal hiatus of the diaphragm

Clinical Manifestations—The para esophageal hernia is usually *asymptomatic* Disturbances secondary to the anomaly rarely appear until later in life when there is senile atrophy of connective tissue surrounding the esophageal opening With this weakening increase in intra abdominal pressure or a change in body posture may force the stomach or some portion of it into the para esophageal space

The symptoms of para esophageal hiatus hernia are often indistinguishable from those of a *typical peptic ulcer* (p 1760) There is usually postprandial pain and when the herniated portion of the stomach ulcerates at the point of constriction there may be *hematemesis* (p 1764) or *melena* (p 1843)

Supradiaphragmatic symptoms may be caused by the para esophageal hernia The postprandial pain may suggest the anginal syndrome or produce *dysphagia* simulating cancer of the esophagus (p 1738) the pains may radiate to arms shoulders or lower thorax

With widening of the hernial orifice there may be complete *eventration* of the abdominal viscera causing physical signs which suggest a tension pneumothorax or pyopneumothorax (p 2035) heart and mediastinum are shifted to the unaffected side and radiography may reveal abdominal organs in the thoracic cavity

Diagnosis—Roentgen examination after a barium meal is necessary for the demonstration of the herniated structures Esophagoscopy may be important as a confirmatory measure

Treatment—Unless the para esophageal hernia gives rise to severe symptoms treatment should be expectant since relief can often be obtained by discovering a position in which the patient may find comfort

With bleeding and intractable pain surgical intervention is required *left phrenicectomy* by elevating the leaf of the diaphragm may give re

The less favorable results of hernial repair in older and obese patients and the possibility for the development of hernial complications impel the practitioner to favor herniorrhaphy in the young patient who is otherwise in good physical condition In obese elderly or handicapped indi







Fig 402—An example of esophagogastric hiatus hernia (Åkerlund type III) in a white woman *sixty three years of age without esophageal or gastric symptoms She was studied* because of diarrhea and lower left abdominal pain due *to diverticulitis The entire* cardiac *end of* the stomach and the abdominal esophagus are above the d aphragm fixed in that position The lower esophagus was redundant The pars cardiaca contains considerable gas

viduals the operative risk must be gauged against the degree of the discomfort and the estimated chance for the appearance of complications Thus incarceration and strangulation are least likely to occur if the hernia has a wide neck The occurrence of complications is less dangerous in

patient feeling the pain and noting the localized swelling of the upper abdomen may force the intestinal contents through the obstruction by massage and manipulation of the abdomen in the region of the swelling

Fluoroscopically the disturbance is characterized by dilatation and hypertrophy of second and third portions of the duodenum with a demonstrable delay at the duodenojejunal flexure

The *treatment* of duodenal obstruction rarely involves surgical intervention When necessary the simplest procedure should be carried out

THE CASCADE STOMACH

The cascade stomach is a familial congenital abnormality that rarely gives symptoms It is more common in women than in men The viscus is divided into two compartments connected by a small channel The fundal



Fig 404—Cascade stomach Note the marked gaseous distention of the splenic flexure

end of the stomach is usually situated anteriorly and laterally to the pyloric half so that the connecting channel runs from left to right and from before backward As a result the patient drains the upper half of the stomach into the lower by lying face downwards with knees bent the right shoulder on the bed and the left shoulder somewhat elevated

Clinical Manifestations—The cascade stomach may never give rise to symptoms On the other hand when sticky foods such as caramels and taffy are ingested or if large chunks of meat are swallowed without being thoroughly masticated the connecting channel is obstructed and a dilatation of the fundal portion of the stomach occurs This is associated with excruciating *left upper abdominal pain* which may radiate to *left shoulder*

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lief to the symptoms of constriction by *intra-abdominal approach* an attempt may be made to repair the opening Operative treatment should be conducted by a surgeon who has had extensive experience in this limited field

EVENTRATION OF THE DIAPHRAGM

Marked elevation of the diaphragm with thinning and relaxation permits abdominal viscera of either side but generally the left to be located in the chest The defect probably is a congenital neuromuscular abnormality the symptoms are those of diaphragmatic hernia and the diagnosis is established by the demonstration of a high arched continuous diaphragm which may have paradoxical respiratory movements



Fig 403 —Showing delay at mid portion of transverse duodenum

Treatment is palliative and consists of the avoidance of conditions productive of increased intra abdominal pressure

HERNIATION THROUGH THE LIGAMENT OF TREITZ

Herniation through the ligament of Treitz is rarely recognized although the manifestations when sought are often quite obvious

Classically the symptoms of herniation are those of intermittent obstruction of the duodenum The patient observes sudden sticking pain in the epigastrium associated with copious vomiting Characteristic of this pain is its occurrence when there is pressure on the abdomen Many sufferers note that the attack is produced by bending over as in tying the shoelaces in the morning A change in position brings relief as is illustrated by the knee chest attitude or lying on the left side Sometimes the

FOREIGN BODIES

All manner of foreign bodies accumulate in the stomach collections of metallic objects have been found in patients with profound psychoses *hair balls (trichobezoar)* may be an unexpected discovery in seeking the cause of an abdominal tumor or obstruction To prevent further damage these abnormal collections should be surgically removed



Fig 405 —Mass of paper clips in stomach



Fig 406 —Phytobezoar with gastric ulcer

GASTRIC DILATATION

Gastric dilatation may result from toxic factors or as a sequel to obstruction Acute gastrectasis is discussed with postoperative complications (p 4004) chronic dilatations accompany pyloric stenosis (p 1789)

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and *arm* Through pressure on the diaphragm there is associated shortness of breath

Examination reveals only the upper abdominal distention If there is an associated weakness of the para esophageal opening the fundal portion may be forced into the thoracic cavity

Treatment —It is rarely necessary to advocate any form of therapy for the cascade stomach other than postural drainage and adherence to a soft diet

CONGENITAL POLYPS

Polyps occur occasionally in the stomach and duodenum more often in the former *They rarely give rise to symptoms unless they become ulcerated and bleed* or undergo carcinomatous degeneration Only when they threaten life or appear precancerous should they be removed by local resection (p 1835)

Diagnosis depends on roentgen studies showing a filling defect The lesion may be observed by gastroscopy

THERMAL INJURY TO THE STOMACH

The stomach and duodenum are protected by the sensitive structures of the mouth from excessively hot or irritating substances Carcinoma of the stomach from the constant ingestion of very hot food has been described by the Chinese

CHEMICAL INJURY TO THE STOMACH

Strong acids and alkalies carbolic acid iodine and bichloride of mercury are sometimes swallowed accidentally or with suicidal intent In addition to local trauma these chemicals produce profound shock which requires emergency treatment (p 928)

A less violent type of chemical irritation results from ingestion of highly spiced and irritating foods from excessive ingestion of alcoholic beverages and from gluttonous overloading of the stomach Relief is afforded by emesis or liberal drinks of warm milk

MECHANICAL DISTURBANCES OF THE STOMACH

Mechanical disturbances of the stomach include penetration and perforation pyloric obstruction and hour glass constriction foreign bodies and gastroptosis

PENETRATION AND PERFORATION

Penetrations and perforations of the stomach result from the ingestion of a sharp or pointed foreign body they also occur at the site of an ulcerous or cancerous lesion (p 1814) *Treatment* involves emergency gastrorrhaphy (p 1758) *measures for the prevention or relief of shock* (p 9°8) topical applications of sulfonamide and parenteral injections of penicillin (p 106)

HOUR GLASS AND PYLORIC OBSTRUCTION

The hour glass and pyloric types of constriction are late *sequels of the* healing of an ulcer they are discussed in the paragraphs on *Complications of Peptic Ulcer* (p 1789)

In more severe instances the process extends deeply into the mucosa and then may involve the submucosa or the entire gastric wall

Etiology—In the majority of patients acute gastritis results from dietary indiscretion the offending foods may be too hot too irritating too highly spiced or incompletely masticated Overdistention of the stomach and erosion by sharp fragments or roughage health foods may produce traumatic lesions

Acute gastritis often represents a local manifestation of a systemic process such as an acute bacterial infection For example in *scarlet fever* the gastric changes are probably similar in nature to the more easily visible alterations in the tongue (p 177) a violent gastritis occurs when *staphylococcus toxin* (p 240) is ingested Acute gastritis may be produced by emotional disturbances and other *psychogenic factors* Inflammation is also associated with the ingestion of *irritant drugs* such as emetics salicylates and concentrated salines used in purging

Clinical Manifestations—Most often the gastroscopically observed changes of acute gastritis give rise to little or no discomfort In those instances with clinical expression *epigastric distress bloating* and *fullness* are noted the stomach feels uneasy *anorexia* is followed by *nausea* and *vomiting* the *tongue* is heavily coated and *salivation* increased

In the more severe and protracted examples *vomiting* is persistent and there are associated systemic manifestations notably *fever* Examination reveals tenderness in the epigastrium The *vomitus* at first contains only food particles and gastric content especially mucus it later becomes bile tinged and streaked with red blood A severe type is most commonly seen in the delicate stomach of infancy and childhood although many adults retain their sensitivity throughout life Alcoholics are particularly prone to a violent form of acute gastritis which may simulate perforation of an ulcer

Secondary to loss of fluid by vomiting urine volume is decreased and concentration increases with recurrent and persistent vomiting *alkalosis* (p 722) develops

Course—In the majority of instances acute gastritis is self limited The patient rapidly recovers an early favorable prognostic sign being the return of appetite In the more severe examples dehydration and disturbances in the electrolyte pattern become increasingly severe unless corrected

Diagnosis—Relatively few instances of acute gastritis are seen by the physician The majority are misdiagnosed and mistreated by well meaning but misinformed members of the household The attack is usually called ptomaine biliousness or acute indigestion and insult is added to injury by the administration of cathartics or purgatives The latter if retained contribute to discomfort and dehydration

The diagnosis of acute gastritis is usually obvious from the history but the practitioner must be wary lest he fall into the error of failing to recognize the more fundamental cause Not content with diagnosing the gastritis he should seek evidence of the onset of an acute infectious disease particularly *scarlet fever* the abdomen is palpated for evidences of intraperitoneal inflammation such as perforation of an ulcer (p 1790) or *acute appendicitis* Despite the history of an alcoholic debauch the possibility of a complicating surgical condition must be considered

GASTROPTOSIS

Gastroptosis is part of the syndrome of generalized visceroptosis (Glenard s disease) The dropped stomach commonly occurs in patients of the ptotic habitus (p 1808) Ordinarily it produces no symptoms However in a certain number of individuals there is an epigastric sensation of dragging particularly after meals appetite is destroyed and due to the mechanical difficulties at the pyloric region there is uncontrollable vomiting and later distaste for food duodenal ileus (p 1804) may be produced by angulation at the duodeno jejunal angle

Patients are helped considerably by strapping of the abdomen and the use of a properly fitting corset or belt containing a kidney shaped pad that fits in the hypogastrium These contrivances force the stomach up into the upper abdomen and straighten out the acutely angulated pyloroduodenal junctions Occasionally a rest cure' with high calory feedings resulting in an appreciable gain in weight is highly efficacious Surgical therapy is not recommended

DUODENAL ILEUS

The syndrome of duodenal ileus is described as it occurs with herniation through the ligament of Treitz (p 1804) Obstruction also may be encountered in functional conditions such as traction in gastrovisceroptosis and acute angulations from whatever cause

ACUTE GASTRITIS

In an earlier period of medical history inflammation of the stomach was regarded as an exceedingly common event The diagnosis of *gastritis* was applied to a great variety of conditions associated with epigastric distress nausea vomiting or the vague clinical syndromes classified as dyspepsia Later in the reign of the organic pathologist there was general agreement that inflammatory disturbances noted in the stomach were agonal preagonal or artefacts due to autodigestion The skepticism of the pathologist concerning the incidence and significance of gastritis resulted in a swing of the pendulum in the direction of denying the frequent or even occasional occurrence of gastritis See Fig 395 p 1745

With the advent of the gastroscope there has been a return to the older ideas It has become apparent that the gastric mucous membrane responds delicately and sensitively to all manner of irritants Changes occur in local vascularity in the outpouring of secretion in the contour of the muscularis mucosa and in the integrity of the lining structures *small erosions are readily and frequently produced* and more *widespread changes* of a transitory or more persistent nature may result from a variety of causative factors Indeed the present tendency exaggerates the importance of gastritis and threatens to lead to over diagnosis Many enthusiastic observers *intimate that functional gastric neuroses are more often than not* based on organic gastric changes

Acute gastritis must occur with great frequency In the majority of instances there are no significant clinical manifestations but gastroscopy reveals *redness injection swelling* exudation of mucus or mucopus and small erosions with blood staining In the milder examples only the superficial layers of the membrane are involved producing *mucous ulceration*

In more severe instances the process extends deeply into the mucosa and then may involve the submucosa or the entire gastric wall

Etiology—In the majority of patients acute gastritis results from dietary indiscretion the offending foods may be too hot too irritating too highly spiced or incompletely masticated Overdistention of the stomach and erosion by sharp fragments or roughage 'health foods may produce traumatic lesions

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Treatment —Gastritis rarely requires more therapy than *avoidance of irritants* Many patients find comfort in sucking *ice* others are benefited by drinking *warm fluids* The *application of heat* in the form of a hot water bottle an electric pad or a pack produces much more comfort than can be explained on physiologic grounds

Abstinence from food is necessary when there is persistent nausea and vomiting Under these circumstances, dehydration of the patient calls for parenteral administration of fluids by intravenous drip (p 3775) In the presence of acidosis dextrose covered by insulin is chosen as the infusate buffer solution is of greatest value when there are manifestations of alkalosis

When the stomach is receptive to food small quantities of bland material are fed promptly and frequently The patient is the best judge of the *time to institute feeding he should be given whatever he thinks might be* palatable some patients do well on cold carbonated fluids such as dry ginger ale or champagne others prefer sips of warm milk, a mushy cereal or mashed potatoes

Drug therapy is limited to the administration of *demulcents* (p) and *protectives* (p 1756) The best demulcent is *milk* preparations of gastric mucin are usually unpalatable though physiologically indicated Of the protectives, *bismuth* and *cerium* salts have the endorsement of usage and may be given in powder form or in a vehicle containing a volatile oil such as

Cerium Oxalate	5 0
Bismuth Subcarbonate	5 0
Cinnamon Water to make	120 0

Sig Shake well and take 1 tsp every 3 hours

CHRONIC GASTRITIS

Chronic gastritis has caused more fruitless discussion than any other condition in clinical medicine anatomic radiographic gastroscopic and symptomatologic findings cannot be correlated Many clinicians believe that chronic gastritis never gives rise to symptoms, others are of the opinion that many of the so-called 'gastric neuroses are in fact evidences of chronic gastritis

Etiology —Chronic gastritis arises from systemic causes as well as local trauma and irritation *Peptic ulcer* and *gastric malignancy* are associated with local inflammatory changes in the mucosa and specific manifestations of gastritis are found in the *avitaminoses* particularly those dependent upon vitamin B deficiency Chronic atrophic gastritis is an *accompaniment of primary anemia* It may result from abuse of the stomach by alcohol coarse food imperfect mastication excessive use of condiments or ingestion of overheated or iced meals The stomach may develop a contactual irritation from allergens similar to a *dermatitis venenata* (p 3330)

Gastroscopic Appearance —The gastroscopist recognizes atrophic and hypertrophic varieties of gastritis In the *atrophic* type the alterations resemble those of the tongue in the glossitis of pernicious anemia the membrane is pale and blood vessels are easily visualized through the thinned

lining membrane there is a tendency to diminished secretion particularly of acid

The *hypertrophic* type assumes a cobblestone appearance due to prominence of the rugae This condition is associated with hypersecretion and shows a tendency toward the formation of peptic ulcer In extreme instances of long duration inflammatory *polyps* develop As a late phase of hypertrophic gastritis an atrophic condition is observed It is not yet clear whether all atrophies are based on initial hypertrophy but there i evidence to suggest that the inflammation represents a *precancerous* condition

Gastritis of varying degree accompanies peptic ulceration and gastric malignancy Often the initial symptoms are related to the gastritis rather than the more important lesion Hence the diagnosis of inflammatory involvement of the stomach is not complete until the more fundamental disturbances have been investigated and found absent

Clinical Manifestations —The *symptoms* attributed to chronic gastritis are varied They include a bad taste in the mouth epigastric fullness and distress discomfort after meals bloating morning nausea and vomiting pyrosis regurgitation of sour fluid (water brash) and loss of weight

Neither physical examination nor radiography is of definitive value in the diagnosis of chronic gastritis The only method by which the diagnosis can be made with assurance is *gastroscopy* by which means atrophic and the hypertrophic types (Fig 395 p 1745) can be recognized Strangely enough these subdivisions cannot be distinguished on the basis of symptoms Likewise there is no correlation between the state of the gastric mucous membrane and the presence or absence of hydrochloric acid in the gastric secretion

Gastric analyses rarely yield information that justifies the trouble and inconvenience to the patient The acid figures may be low or high Gastric mucus may be increased or decreased in amount and tenacity Traces of blood may be demonstrable by chemical tests

In the instance of an anacidity injection of *histamine phosphate* (p 3890) is desirable complete achylia after the injection of the drug requires more extensive examination for the possible presence of a *primary anemia* (p 1077) or a *gastric malignancy* A complete *blood count* should be re recorded and a *radiographic examination* is conducted by the specialist radiologist *Stool examinations* are made for occult blood for at least three days while the patient is on a meat free diet If the suspicion of *malignancy* cannot be definitively allayed gastroscopy or laparotomy is desirable

Treatment —The treatment of chronic gastritis is most unsatisfactory unless the etiologic agent is discoverable and curable In avitaminoses or primary anemia therapy is directed at the more fundamental condition despite the fact that gastroscopic examination shows no gross change in the mucosa after intensive treatment

Local Measures —The local treatment of chronic gastritis is varied and diversified With a low or absent acidity *hydrochloric acid* (p 1778) *is* administered with the higher acid figures *antacids* (p 1754) and *protectives* (p 1756) are desirable *gastric lavage* (p 1749) is recommended if the secretion is tenacious and there is evidence of retention

Dental Hygiene—Dental hygiene requires conscientious attention Patients are urged to masticate thoroughly and eat slowly A type of gastritis that is *not too uncommon occurs in the edentate* (p 1680) The swallowing of pus from a postnasal drip or a pyorrhea alveolaris may contribute to the inflammation

Diet—It is doubtful whether diet plays an important role in the treatment of chronic gastritis other than to see that there is no continued irritation Alcohol condiments raw and uncooked foods high seasoning and bizarre edibles are banned In essence the diet is smooth bland cooked and mixed (p 668) Greasy and fried foods extremely hot and excessively cold courses should not be permitted candy and syrups are very likely to cause difficulty The physician should inquire into the eating habits and routines of the patient and his household and attempt to suit the diet to the patient s way of life'

If possible the meal is eaten in peace and quiet The patient does well to lie down for thirty to sixty minutes after the repast with an *electric pad* or *hot water bottle* over the epigastrium Patients who are most disturbed by morning nausea and vomiting often obtain great comfort from the habit of drinking a glass of warm water with a pinch of *bicarbonated soda* dissolved therein others begin the day with *lemon juice*

Alcohol—The wisdom of using alcohol is controversial certainly gastritis may result from the ingestion of alcoholic beverages nevertheless there are certain symptoms particularly anorexia and bloating which respond well to the temperate use of liquor The most efficient and pleasant appetizer is a cocktail such as the martini the old fashioned or a whiskey sour After dinner emptying of the stomach is hastened and distress is relieved through the sipping of a liqueur preferably one containing peppermint

Water—Contrary to general belief ingestion of large quantities of water is not recommended The patient should be guided by his thirst The stomach is apt to be distended if the current vogue for forcing fluids is followed

Constipation—Constipation definitely effects the symptoms referable to *reverse peristalsis* (p 1778) in chronic gastritis A daily evacuation in the morning hours is to be encouraged Failing this stool may be obtained by the insertion of a glycerin suppository or a small rectal flush The use of cathartics particularly the drastics is not favored since violent peristalsis is apt to upset the stomach

Sedation—Sedation is often of greater value than the medication directed toward the stomach itself our own preference is for *Mistura Nigra* (p 1757)

Miscellaneous—Systemic therapy should include the administration of vitamin B complex *With any suspicion of the prodromal phases of* a primary anemia injections of *liver extract* are distinctly in order

With the persistence of symptoms general physical and mental hygiene require attention a rest cure either complete or partial a vacation or holiday *or hospitalization under the Weir Mitchell regimen* (p 3754) may be necessary if present symptoms are to be allayed and future complications prevented

PHLEGMONOUS GASTRITIS

Phlegmonous gastritis a severe inflammation of the stomach is probably caused by the *hemolytic streptococcus* It may be associated with streptococcal diseases such as scarlet fever erysipelas or osteomyelitis rarely it is observed in *diphtheria*

The *suspicion of the presence of a phlegmonous gastritis* arises when in the course of a bacteremia or septicemia the patient complains of severe nausea vomiting epigastric pain and tenderness the temperature level rises intermittent chills are experienced and manifestations of toxemia and shock are noted

The treatment of phlegmonous gastritis requires withholding of food and the institution of a *continuous intravenous drip* Specific anti infective measures are inaugurated using *sulfonamide* (p 88) and/or *pen*

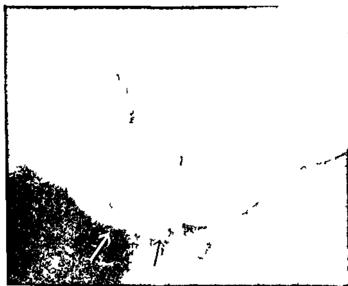


Fig 407—Two polyps of the stomach

icillin (p 106) for streptococcal infection and *diphtheria antitoxin* (p 310) when the complication arises in the course of an infection with the Klebs Loffler bacillus

DUODENITIS

Duodenitis is probably more common than is generally believed It is invariably an accompaniment of *duodenal ulcer* (p 1780) and also occurs as a result of *angulation of the duodenojejunal junction* (p 1804) It may be associated with catarrhal jaundice (p 1979) since the latter is preceded by a prodromal period of upper intestinal distress and dysfunction

DUODENAL DIVERTICULA

Small duodenal diverticula are frequently found radiographically along the mesial border of the second portion They rarely cause symptoms and require no treatment

Buckstein Clinical Roentgenology of the Alimentary Tract

BENIGN TUMORS OF THE STOMACH

Benign neoplasms of the stomach include *fibroma myoma fibromyoma neurofibroma hemangioma lymphoblastoma adenoma* and *polyps* which may be single or multiple

Benign gastric tumors do not cause symptoms unless they become ulcerated and produce *hematemesis or melena* Under these circumstances a malignant lesion is suspected at operation the surgeon is delighted to find that he is dealing with an innocent growth Single or isolated tumors are removed with the adjacent portion of the stomach in multiple polyposis however malignant degeneration sometimes occurs and a radical *subtotal gastrectomy* is worthy of consideration

DIFFERENTIAL DIAGNOSIS OF

Epigastric Swellings and Tumors

Swellings and tumors in the epigastrium are often difficult to delineate For accurate identification it may be necessary to attempt to visualize stomach colon gallbladder and urinary passages by direct and contrast radiography

SWELLING	DIAGNOSTIC FEATURES
Xiphoid	Particularly with enlarged cartilage in a lean individual
Gastric	With dilatation confirmed by gastric aspiration (p 1751) Congenital hypertrophic stenosis in infancy Malignancy in the adult Get gastric analyses (p 3722) and barium meal
Colonic	Spasm or neoplasm of transverse colon Confirm by barium enema (p 1824) and repeated examinations of stool for occult blood (p 3728)
Hepatic	See Hepatomegaly (p 1973)
Pancreatic	Cysts and neoplasms Diagnostic laparotomy
Splenic	See Splenomegaly (p 1129)
Renal	Particularly Wilms tumor in infancy Horseshoe kidney Confirm by intravenous urography (p 2251)
Circulatory	Pulsations of dynamic aorta in lean individuals Aneurysm of abdominal aorta producing expansile pulsation

CARCINOMA OF THE STOMACH

Carcinoma of the stomach is one of the most common malignant lesions observed in patients beyond middle life although it may occur at any age its course is most rapid in younger individuals Its incidence is not sex linked but examples are more frequently encountered in males

Pathology—Malignancies of the stomach are of scirrhous or medullary types The *scirrhous carcinoma* has a tendency to produce lymphatic destruction and an excessive formation of fibrous tissue As a result the entire wall of the stomach may become infiltrated forming the so called leather bottle (*linitis plastica*)

In the *medullary type of carcinoma* the lesion is apt to be localized and forms a filling defect which can be seen radiographically The medullary carcinoma tends to ulcerate in its center and closely resembles a peptic ulcer Some believe that ulcerating medullary carcinoma starts as a peptic ulcer while others including the authors are not at all convinced that the simple peptic ulcer ever assumes malignant characteristics The cell types associated with medullary carcinoma are glandular (*adenocarcinoma*) or epithelial (*alveolar*) Each produces large amounts of mucus and metastases in the peritoneum are characterized by large masses of gelatinous colloid

Carcinomas may be cauliflower or polypoid ulcerous mushroomlike or flat they are generally located at the pylorus and then in order of fre

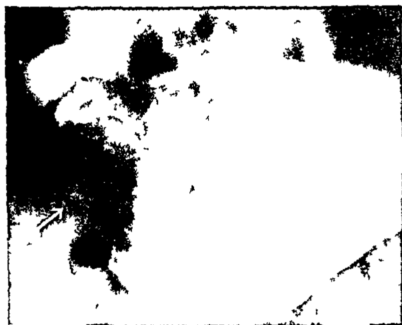


Fig 408 —Adenocarcinoma of the stomach

quency at lesser curvature cardia greater curvature posterior wall and anterior wall Except for surmises concerning the malignant degeneration of chronic gastritis polyps and adenomas the etiology of gastric carcinoma is unknown

Clinical Manifestations —The symptoms of cancer of the stomach are variable and may be predominantly gastric or extragastric *Gastric symptoms* are usually insidious but may be sudden and severe when the ulcerating neoplasm produces *hematemesis melena* or *perforation* More often the presenting complaint is progressive *anorexia distaste for food nausea* or postprandial *pain* suggestive of a peptic or arteriosclerotic ulcer Large lesions at the *cardia* produce difficulty in *deglutition* resembling a cardiospasm or an inflammation of the lower portion of the esophagus A

* Buckstein Clinical Roentgenology of the Alimentary Tract

growth at the *pylorus* produces the symptoms of an *obstruction* with gastric retention and persistent vomiting

The *extragastric* symptoms of cancer of the stomach are most confusing and ominous since they usually indicate that metastasis has occurred and *operability is no longer possible* *There may be nonspecific generalized* symptoms such as an inexplicable *secondary anemia fever leukocytosis* and increase in the sedimentation rate On other occasions the hemogram reveals a *hyperchromic type of anemia* identical with that seen in the pernicious form (p 1077) *With dietary restriction of* protein the patient may develop a generalized *anasarca* as in nephrosis (p 717)

Metastatic involvements may be herald manifestations With *miliary carcinomatosis of the lung* the presenting syndrome is respiratory with dyspnea cough fever and radiographic evidences of widespread infiltration Implants in *bone* particularly the spine cause pain and disability Obstruction of the *thoracic duct* produces a *chylous ascites* (p 1921) as the predominating disturbance

Physical examination may reveal metastatic deposits in distant places The *Virchow node* in the supraclavicular region may be a chance finding The physician may palpate infiltrations in the *rectovaginal* or *rectovesical* cul de sac as evidences of peritoneal invasion (*Blumer's shelf*) The *Krukenberg tumor* of the ovary results from hematogenous metastasis giving rise to bilateral *adnexal swelling* Occasionally the diagnosis is made by a routine examination of the epigastrium which reveals the presence of a large mass (p 1814)

Laboratory Tests—Laboratory examinations are often helpful in the diagnosis of gastric cancer *Gastric analysis* reveals a subacidity or an achlorhydria with high total acidity With ulceration coffee ground contents are obtained In the absence of hydrochloric acid and with retention lactic acid and Boas Oppler bacilli are demonstrable Examination of the *stool* for occult blood reveals persistent positive tests with ulcerating lesions but negative results are obtained when the carcinoma is of the scirrhous variety

Gastro intestinal *radiography* is indicated upon slight suspicion For this examination the patient is best referred to the specialist since small lesions in silent areas, such as the cardia are difficult of demonstration

The innovations of *gastroscopy* (p 1745) and *electrogastrography* (p 1747) promise more definitive diagnosis of gastric cancer Through the use of the gastroscope the expert not only visualizes the lesion but may obtain a *biopsy specimen Electrogastrograms* may furnish a specific curve for early establishment of the diagnosis

Diagnosis—The astute practitioner will entertain a high index of suspicion relative to cancer of the stomach An extensive survey is warranted when any middle aged patient develops anorexia *gastric distress* or otherwise inexplicable loss of weight It is well worth hundreds of unnecessary gastric analyses and radiographic examinations to gain the opportunity of operating on one of these malignancies in the early stage

With progression of symptoms and inconclusive laboratory examination an *exploratory laparotomy* is justifiable If operative intervention is postponed until the mass is palpable or metastases are demonstrable the slim chance for cure is sacrificed Despite all of the clinical criteria

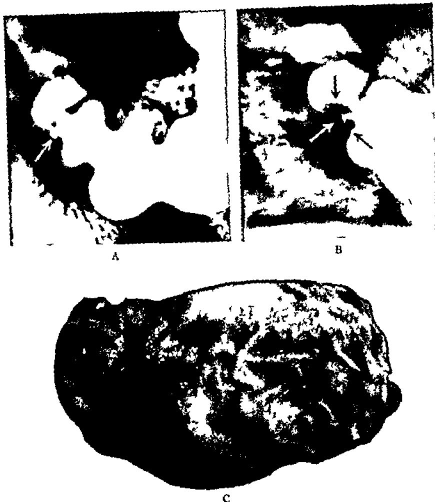


Fig 409—A woman forty four years of age with a h story of se eral attacks of pain in the upper right quadrant dur ng the previous two years was admitted to the Graduate Hospital of the Uni ers ty of Pennsyl ania two weeks following an attack of mod rate hemat eme is After the bleed ng episode ulcer l ke symptoms pers ste l up to the time of admission The fract onal ga tric analysis showed a gastric hyperac d ty *A* X ray exam nation Feb 25 1942 (soon after adm ss on) clearly demonstrated an ulcer niche project ng from the greater curvature of the stomach about 5 cm from the pylorus The n che was a sociated with an annular constr ction which was pers stent *B* A therapeut c tr l on a strict ulcer reg men for two w ks was followed by a second roentgen stu ly on Mar h 9 1942 The niche appeared som hat smaller but the annular constr ction pers ste l and was constant throughout the fluoroscopy Furthermore there w s a ugg st on of a finger impress on type of subtraction defect on th gr ater curvature sid from which the ulcer seemed to ar se *C* At subtot l resection perforn d by W F Lee a ery innocent almost healed small ga tr c ulcer was found A crease in the muco a completely enc rcled the stoma h at the site of the ulcer The color photograph beautifully shows the cause for the apparent filling defect—a large redundant fold of mucosa between the ul er and the pylorus The micro copy of the sections revealed no sign of mal gnant disease



Fig 410—A circumscribed lymphosarcoma in a man twenty three years of age involving the lower part of the body of the stomach *A* The prone oblique film may be considered to show no abnormality The duodenal cap and pars pylorica appear normal *B* The supine film demonstrates a large oval translucent filling defect in the body of the stomach with a large circumscribed irregularly oval collection of barium in its central portion The filling defect with its central crater is an exact roentgen reproduction of the gross morphologic character of the tumor with its large irregular surface ulceration (*C*)

by which peptic ulcer is said to be differentiated from malignancy the only sure method of diagnosis involves exploratory laparotomy and section of the suspicious area

* Bockus Gastro-enterology Vol I

Prognosis and Treatment.—The only treatment that holds any promise of relief in cancer of the stomach is early *subtotal gastrectomy* (p 1760). Unfortunately even with skillful diagnosis and expert surgery the long range outlook is most discouraging. The average duration of life following operation is less than two years and five-year survivals are indeed unusual. *Roentgen therapy* is of no value and *implantations of testicular extract* (p 2404) in our experience hold little promise.

MYOSARCOMA OF THE STOMACH

Extragastric myosarcoma has certain unusual and pathognomonic characteristics which frequently permit of ante-operative diagnosis. The neoplasm arises as a small lesion of the gastric wall. It penetrates into the peritoneal cavity where it may grow to be so large that it simulates an *ascites* or an *ovarian cyst* (p 2576). The extragastric compartment contains hemorrhagic fluid and presents itself as a huge mass which shifts as the patient moves. *Abdominal tap* intended to drain the peritoneal cavity yields bloody material derived from within the cyst.

Clinical Manifestations.—The symptoms are usually vague and consist of gastric distress. At times the lesion ulcerates and produces a massive gastric *hemorrhage* but the striking characteristic is the enormous size of the tumor with the relatively slight subjective disturbances.

Diagnosis and Treatment.—Recognition of gastric myosarcoma is of importance since wide excision of the stomach and its attached mass holds great promise for radical cure. Roentgen therapy is valueless both in regard to the original lesion and recurrences.

CHAPTER 91

THE INTESTINES PHYSIOLOGY METHODS OF DIAGNOSIS AND TREATMENT

ANATOMY

See p 3569

THE PHYSIOLOGY OF THE INTESTINES

The *small bowel* and the *right half of the colon* derived from mid gut form a unit serving for digestion and absorption the *left half of the colon* of hind gut origin from the middle of transverse portion to anus is concerned mainly with fecal excretion Neoplasm occurring in the two regions manifest characteristic differences

The intestines have a multiplicity of functions Among these are motor digestive absorptive excretory and hormonal activities

Motor Function—The small bowel has at least three types of motor activity *segmental contractions* knead mechanically manipulate and subdivide intestinal contents *pendulum movement* shifts food backward and forward through a loop hastening enzymatic break down finally *peristalsis* propels the column of food from duodenum to ileum a passage which usually consumes six hours with frequent variations

In the *large bowel* the *haustra* grasp small amounts of fecal materials and retain them until useful matter is absorbed dried material is then discharged into the main lumen of the colon Changes in tonus serve to bring colonic contents into more intimat contact with the mucous membrane and mass movements by spastic diminution in caliber over distances of 15 to 20 cm propel intestinal content into more distal portions of the colon eventually giving rise to the desire for *defecation* The colonic mass movements initiated by the sight smell or ingestion of food probably occur through a direct neural mechanism without hormonal intermediation Abnormally retrograde peristalsis occurs in the colon

The motor nerve to the bowel is *cholinergic* hence physostigmine and its substitutes are powerful therapeutic agents in intestinal paresis and toxic ileus

Digestion—The digestive processes in the small intestines occur in concert with motor and absorptive processes Digestion is accomplished by *enzymes* which convert various types of food into products that are capable of absorption The motor function brings the mucous membrane into intimate contact with the semifluid mass of food material villi increase fifteenfold the secreting surface by means of their varying sizes shapes and continuous movements

Fat—The digestion of the fats is carried out through *biliary and pancreatic secretions* which are discharged from the common bile duct into second portion of duodenum *Bile salts* emulsify fat and render it more readily accessible to the digestive action of pancreatic *steapsin*

Protein—Protein digestion is effected through *trypsin* and *erepsin* The former is derived from its precursor pancreatic *trypsinogen* activation occurring on contact with duodenal *enterokinase* Trypsin converts protein to the *polypeptide stage* the final protein break down to amino acid being accomplished by *erepsin* in the lumen of the lower portion of small bowel

Starch—*Pancreatic amylase* converts starchy foods to the dextrins which are hydrolyzed into glucose preparatory to absorption

Absorption—The absorption of the various foodstuffs is subject to considerable variation Ingested *glucose* is probably absorbed in the duodenum starch is hydrolyzed to glucose in the lower portion of th small intestine where absorption then takes place *Fats and protein* ar probably absorbed in the lower portion of the small bowel and the right half of the colon which also functions actively for water absorption

Factors Influencing Absorption—The absorptive functions of the bowel depend upon several variables other than the integrity of the mucous membrane When the small intestine (which is normally slightly acid) becomes alkaline *iron salts* are not absorbed and a secondary anemia may develop On this observation is based the necessity for the use of hydrochloric acid with hematinics (p 1049) In the absence of *vitamin D calcium* is not absorbed and metabolic disturbances such as rickets are initiated In the absence of *bile salts* fat soluble *vitamins A D and K* are not absorbed and specific avitaminoses are produced

The absorption of salt glucose and amino acids is mainly accomplished by osmotic phenomena but some additional process may be performed by cells of the intestinal mucous membrane

Excretion—The small intestine excretes varying amounts of *fat* which are then reabsorbed in the lower loop In addition the small bowel casts off surface epithelial cells which are regenerated from the bases of the glands and a large number of blood cellular constituents especially of the lympho ytic series Foreign substances particularly *heavy metals* are also excreted by the bowel producing conditions such as th toxic enteritis and colitis of mercury poisoning

The *left half of the bowel* serves mainly for the propulsion of the fecal mass

Hormonal Activity—The small intestine has important endocrine functions When hydrochloric acid comes in contact with the duodenal mucous membrane it liberates *secretin* which upon circulating through the blood reaches pancreas and stimulates the output of pancreatic ferments In addition to secretin the bowel puts forth *enterocrinin* which increases the flow of succus entericus and *villikinin* which controls the movement of the villi

Entero astrone is an intestinal internal secretory product which inhibits gastric motility and the *secretion* of hydrochloric acid Urogastrone similar to it is found in the urine it has been used experimentally to inhibit the *formation of the Mann Williamson peptic* ulcer Anthelone from pregnant urine produces like effects

BACTERIOLOGY OF THE BOWEL

Approximately half the weight of the stool is due to bacterial bodies Since few bacteria can resist acid reaction and the digestive processes of the upper bowel the enormous bacterial flora must arise from small intestines and colon which act as gigantic culture media

Normal Flora—Under ordinary circumstances *colon bacilli* constitute 60 to 90 per cent of the intestinal flora Other organisms that are frequently found include *B mucosus capsulatus acidophilus enterococci* and *anaerobes of the Welch variety yeasts* and *molds* are sometimes present in the upper intestinal tract but they *do not occur very frequently in the stool Protozoa* such as *Balantidium coli* and *Endamoeba coli* are also *recognized*

Pathogenic Inhabitants—Healthy individuals in a carrier state may harbor pathogens such as paratyphoid typhoid and *dysentery bacilli Viruses* also may survive in the colonic test tube and transmit such diseases as poliomyelitis

Physiology of Fecal Bacteria—Intestinal bacteria serve a useful physiological purpose—illustrated by the fact that the newborn cannot survive if the intestinal tract is sterile In *this sense* it may almost be said that man is essentially a parasite dependent upon his fecal organisms

Food Poisonings and Ptomaine Poisoning—Intestinal micro-organisms may produce acute and *chronic local* disturbances infections and infestations The *acute upsets* ar commonly labeled food poisoning or ptomain These terms are misnomers since the vast majority result from *absorption of staphylococcic enterotoxin* (p 240) or from infections with *salmonella* (p 239) More violent effects fortunately rare ar produced by the *botulinus* toxin

Autointoxication—A frequent and vague type of bacterial toxemia is the condition labeled auto-intoxication" Though many trained clinicians deny th existence of this state others including the present authors are firmly convinced of its existence frequency and importance

CHAPTER 91

THE INTESTINES PHYSIOLOGY METHODS OF DIAGNOSIS AND TREATMENT

ANATOMY

See p 3562

THE PHYSIOLOGY OF THE INTESTINES

The *small bowel* and the *right half of the colon* derived from mid gut form a unit serving for digestion and absorption the *left half of the colon* of hind gut origin from the middle of transverse portion to anus is concerned mainly with fecal excretion Neoplasm occurring in the two regions manifest characteristic differences

The intestines have a multiplicity of functions Among these are motor digestive absorptive excretory and hormonal activities

Motor Function —The small bowel has at least three types of motor activity *segmental contractions* knead mechanically manipulate and subdivide intestinal contents *pendulum movement* shifts food backward and forward through a loop hastening enzymatic break down finally *peristalsis* propels the column of food from duodenum to ileum a passage which usually consumes six hours with frequent variations

In the *large bowel* the *haustra* grasp small amounts of fecal materials and retain them until useful matter is absorbed dried material is then discharged into the main lumen of the colon Changes in tonus serve to bring colonic contents into more intimate contact with the mucous membrane and mass movements by spastic diminution in caliber over distances of 15 to 20 cm propel intestinal content into more distal portions of the colon eventually giving rise to the desire for *defecation* The colonic mass movements initiated by the sight smell or ingestion of food probably occur through a direct neural mechanism without hormonal intermediation Abnormally retrograde peristalsis occurs in the colon

The motor nerve to the bowel is *cholinergic* hence physostigmine and its substitutes are powerful therapeutic agents in intestinal paresis and toxic ileus

Digestion —The digestive processes in the small intestines occur in concert with motor and absorptive processes Digestion is accomplished by *enzymes* which convert various types of food into products that are capable of absorption The motor function brings the mucous membrane into intimate contact with the semifluid mass of food material villi increase fifteenfold the secreting surface by means of their varying sizes shapes and continuous movements

Fat —The digestion of the fats is carried out through *biliary and pancreatic secretions* which are discharged from the common bile duct into second portion of duodenum *Bile salts* emulsify fat and render it more readily accessible to the digestive action of pancreatic *steapsin*

Protein —Protein digestion is effected through *trypsin* and *erepsin* The former is derived from its precursor pancreatic *trypsinogen* activation occurring on contact with duodenal *enterokinase* Trypsin converts protein to the *polypeptide stage* the final protein break down to amino acid being accomplished by *erepsin* in the lumen of the lower portion of small bowel

Starch—*Pancreatic amylase* converts starchy foods to the d xtrins which are hydrolyzed into glucose preparatory to absorption

Absorpt on—Tl absorption of tl e various foodstuffs is subject to cons derable variation Ingested *glucose* is probably absorbed in the luodenum starch is hydrolyze l to glucose n the lower portion of the small intestine where absorption then takes place *Fats a d protein* are probably absorbed in the lower portion of the small bowel and the right half of the colon which also functions actively for water absorption

Factors Influencing Absorption—The absorptive functions of the bowel depend upon se eral variables other than the integrity of the mucous membrane When the small ntestine (which is normally sl ghtly aci l) becomes alkaline *iron salts* are not absorbed and a s condary anemia may develop On this observation is based th necessity for the use of hydrochloric acid with h matinics (p 1049) In the absence of *vitam n D calcium* i n t absorbed an l m tabol c d sturbances such as rickets are in tiated In the absen e of *bile* s its fat soluble *vitamins A D and K* are not absorbed and sp cific avitam noses are produced

The absorption of salt, glucose and am no acids is mainly accomplished by osmotic phe omena but some add tional process may be performed by cells of tl e intest nal mucous membrane

E et on—The small intestine excretes varying an ounts of *fat* which are then reabsorbed in the lower loop In addition the small bowel casts off surface epithelial cells which a e regenerat d from the bases of the glands and a large number of blood cellular con stituents especially of the lymphocytic series Fore gn substances partı ula ly *l eavy metals* are also excreted by the bowel producing cond t ons s ich as th toxic ent ritis and colitis of mercury po soning

The *le't ha'f of the bowel* serves mainly for the propulsi n of the fecal mass

Hormo al Act vity—Tl e small intestine has *important endocrine functions* When hydrochloric acid comes in contact with the duodenal mucous membrane it l berates *secretin* which upon circulating through the blood reaches pancreas and stimulates the output of pancreatic ferments In addition to secretin the bowel puts forth *enterocrinin* which increases the flow of succus entericus and *villikinin* which controls the movement of the villi

Enterogastrone is an intestinal internal secretory product which inhibits gastric motility and the secretion of hydrochlo ic ac d Urogastrone similar to it is found in th ur ne it has been used experimentally to inhil t the formation of the Mann Williamson peptic ulcer Anthelon f om pregnant urine produces l ke effe ts

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Infections and Infestations—Intestinal infections and infestations are usually but not invariably food borne *hookworm* is introduced through the soles of the feet and the enteric lesions of tuberculosis are lymphogenous The prevention and treatment of these conditions must not be limited to the attack on the intestine but must be conducted along broader lines

Intestinal bacteria present a problem for the surgeon who contemplates resections of the gut The risk of soiling the peritoneum is greatly decreased by preliminary *prophylactic chemotherapy* with insoluble sulfonamides such as *sulfaguanidine sulfathaladine* and *sulfasuxidine* (p 100) and by injections of penicillin and streptomycin (p 103)

EXAMINATIONS OF SMALL BOWEL AND COLON

Physical Examination—Routine investigation of small and large intestines is carried out by abdominal and rectal palpation and by abdominal auscultation At times palpation is made easier by examining the patient in a warm bath where relaxation is more complete

Abdominal palpation (p 3552) often reveals tenderness over spastic bowel particularly in cecal and sigmoidal regions The constricted gut must not be mistaken for an *abdominal tumor* (p 1886) In instances of doubt a complete *roentgenologic investigation* is required both before and after the use of antispasmodics (p 3892) *Abdominal tenderness and rigidity* (p 1746) suggest peritoneal irritation Violent gurglings revealed by auscultation indicate *organic obstruction* (p 1873) and complete quiet suggests a *paralytic ileus* (p 1851) Rectal examination may disclose a palpable mass or local erosion and ulceration

Laboratory Investigations—Most important evidence regarding the bowel is obtained from *stool examinations* (p 3721) despite the nuisance for patient and examiner Persistence of *occult blood* (p 3728) after a meat free diet is reliable evidence that there is an ulcerating lesion of the bowel *ova* and *parasites* may be discovered in fresh preparation and the Gram stain reveals the nature of the *bacterial flora* (p 1821) cultures are required for the diagnosis of enteric fevers and the dysenteries

Examinations of the *duodenal content* are useful in biliary tract disorders (p 3726) pancreatic ferments are absent only in advanced disease

Proctoscopy and Sigmoidoscopy—Proctoscopy and sigmoidoscopy (p 1907) are performed with considerable ease and safety if precautions are carefully followed Visual examinations give information of value concerning the appearance of the mucous membrane of the lower bowel specimens can be obtained for bacteriology warm stage examination and biopsy

Roentgenography—Roentgenograms of the gastro intestinal tract are of the greatest value Preliminary or scout films are taken in anteroposterior and postero anterior positions The former give evidence of distention of the bowel the presence of calculi and distortions of renal shadows the postero anterior film if focused over the region of the gallbladder often reveals the characteristic shadows of gallstones Scout films are supplemented by the use of contrast media the gastro intestinal tract is studied from above with the *barium meal* and from below with the *barium enema* The *gallbladder* is outlined by the excreted dye (p 2000)

An examination of limited value is *pneumoperitoneum* in which x rays are taken after air has been injected into the peritoneal cavity

Bacteriology and Warm stage Microscopy—Whereas routine surveys of stool and duodenal contents can be carried out by the practitioner in his

laboratory bacteriologic and warm stage examinations require expert assistance The growth of enteric pathogens requires the use of differential media (p 54) specimens must be concentrated before making the carbolfuchsin stain for tubercle bacilli (p 52) *warm stage* examinations for *Endamoeba histolytica* (p 523) require expert knowledge to differentiate harmless *Endamoeba coli* and the pathogenic organism of amebic dysentery

The Consulting Surgeon —The specialist surgeon assists in diagnosis by performing an abdominal puncture or an exploratory laparotomy *peritoneoscopy* (laparoscopy) is still an experimental method

Abdominal Puncture—Abdominal puncture may save unnecessary laparotomy or indicate the urgent necessity for surgical intervention

The *technic* consists in the introduction of a needle into the peritoneal cavity and aspiration through an attached syringe The patient voids or is catheterized and the abdomen is prepared with iodine and alcohol After superficial procaine anesthetization a lumbar puncture needle with stylet is introduced bevel down into the skin The abdominal wall is penetrated slowly and the peritoneal cavity entered It is advisable to direct the needle obliquely (i e making an angle of about 70 degrees with the abdominal wall) since this minimizes the danger of perforating hollow viscera The site of puncture depends upon the suspected location and nature of the pathological process One or all four abdominal quadrants may be used

Once the peritoneal cavity is entered the stylet is removed and a syringe is attached to the needle Exploratory aspiration is commenced

Exploratory Laparotomy—Exploratory laparotomy is required when the suspicion of malignancy cannot be allayed and when suppurative infection is probable The risk is comparatively small compared to the ominous consequences of procrastination

SPECIAL METHODS OF TREATMENT FOR SMALL BOWEL AND COLON

Mechanical pharmacologic and surgical methods are employed in the treatment of the hollow bowel

Intestinal Intubation Decompression and Drainage

The *Miller Abbott tube* has revolutionized the treatment of intestinal disorders The tube simultaneously decompresses the gut drains intestinal content and stimulates the bowel to peristaltic action

The Miller Abbott apparatus consists of a long double barreled tube slightly thicker than that used in the duodenum The proximal end of the tube has separate openings for the inner and outer lumina The *outer tube* functions through perforations at its tip for aspiration or continuous suction of intestinal contents The *inner tube* is employed to provide a stimulus to peristalsis by means of an inflated balloon The intestinal movements carry the tube down the lumen of the bowel toward the site of the obstruction

The inner tube which ends just short of the outer portion has a series

of perforations that traverse both the inner and outer coats near the distal end but proximal to the outlet of the outer layer The inner tube apertures are closed off by a small balloon improvised by snipping off the end of a condom and lashing the end firmly to the tubing by means of thread

For the performance of *intubation of the small intestines* the balloon is deflated and the tube is lubricated throughout its length It is passed through the nose or mouth to the 45 cm mark The patient lies on the right side and swallows the tube inch by inch When the duodenum has been successfully entered (as evidenced by the failure to aspirate a solu tion of methylene blue that is taken by mouth) air is injected into the inner tube in order to inflate the balloon Meanwhile continuous suction and repeated aspiration are applied The stimulus of the balloon carries the tube toward the rectal end of the intestinal tract while the outer tube provides continuous drainage and decompression of the dilated bowel

The introduction of the Miller Abbott tube has reduced operative mor tality when surgery is mandatory It has lessened the number of surgical procedures by effecting relief of the obstruction as the result of decom pression of the bowel

Enemas Colon Irrigations and Proctoclyses

Enemas colon irrigations and proctoclyses are nursing procedures al though occasionally the practitioner administers them Often he teaches the technic to a patient or a member of the family

The enema may be of the cleansing or retention type The *retention enema* is usually composed of 1 or 2 ounces of olive oil The *cleansing enema* is most simply accomplished with soapsuds and water The patient lies on the back or the left side A medium sized hard rubber tip is inserted after lubrication within the anal orifice The fluid is permitted slowly to enter the bowel The flow is interrupted on complaint of cramping It is resumed when the spasm relaxes As soon as the patient notes fulness the enema is stopped The patient attempts to hold the fluid for a few moments before evacuation

Individuals vary in the amount of fluid taken and the time that it is held In the barium enema as observed by fluoroscopy the normal bowel will usually hold 1 to 2 quarts The opaque mixture rapidly passes through the bowel and reaches the cecum within a few seconds or at the most minutes

The differentiation between *high* and *low* enemas appears to be quite meaningless since the fluid reaches the cecum without reference to the amount of tubing inserted into the rectum

Very little is accomplished by the enemas made up of more complicated fluid than soap and water The addition of glycerine asafetida epsom salts and other counterirritants such as the volatile oils actually accomplishes little purpose In the presence of marked atony of the bowel or when the patient cooperates poorly and will not retain a large amount of fluid the old fashioned milk and molasses enema is often highly effectual This is readily prepared by adding a glass of warm milk to a glass of warm mo lasses The mixture is permitted slowly to enter the rectum The result is usually most effective

The colon irrigation enjoys wide popularity in the larger centers where

institutes for the conduct of this form of therapy are readily available The irrigation may be effected with the aid of complicated and expensive apparatus or it can be carried out in the home by means of a Y tube or a T tube If the T tube is to be employed the ordinary rectal tip is passed into the anal orifice When the Y tube is used a smaller catheter for inflow is threaded through a larger rectal tube that is used for the outflow

The colon irrigation is preceded by a cleansing enema Thereafter the bowel is washed with several gallons of fluid usually saline solution or a weak bicarbonate

It is very difficult to evaluate the efficacy of the colon irrigation Enthusiasts claim for it extraordinary results in the treatment of local disturbances in the bowel and systemic complaints allegedly due to so called auto intoxication How much more is accomplished by the irrigation than by the simple enema is difficult to decide Certain it is that many physicians and patients are convinced that the colon irrigation is a potent and valuable therapeutic measure

Proctoclysis or the *rectal infusion* provides a method for the administration of fluid particularly when the patient has disturbances in the upper digestive passage The ordinary enema bag may be employed It is filled with saline bicarbonate or glucose solution which is dripped into the rectum through a small catheter at the rate of approximately 2 cc per minute

Local and Topical Medicaments

Local and topical medicaments may (1) alter fecal contents (2) act upon the intestinal membrane and (3) cause destruction and elimination of intestinal parasites

Petrolatum (Mineral Oil) —Petrolatum lubricates the stool and prevents excessive dehydration in the colon it is prescribed as the *Petrolatum Album U S P* (*white petrolatum*) *Liquid Petrolatum U.S.P* (*white mineral oil*) and *Emulsion of Liquid Petrolatum U.S.P* Russian oils have no advantage over American oils and are considerably more expensive proprietary mineral oil preparations contain flavoring and coloring matter and cathartics such as phenolphthalein milk of magnesia or cascara

The *mineral oils* are given in doses of 15 to 60 cc Their action is purely mechanical They are not habit forming but they may dissolve certain of the vitamins particularly A with resultant deficiency symptoms (p 619) Large doses result in seepage and soiling but otherwise there are no untoward effects

For obese patients on a low calory diet (p 669) the mineral oil may be prescribed in the form of a mayonnaise prepared by the addition of mustard pepper salt and other condiments to taste

Bran Agar and Irish Moss —The bulk of the stool may be increased by the administration of inert indigestible *cellulose* or *hemicellulose* (p 588) To produce a stool of sufficient bulk to stimulate peristalsis and defecation approximately 15 gm of fiber must be ingested daily by the normal adult Due to refinement of diet and the use of concentrated foods there is often insufficient bulk for successful evacuation bulk may be supplied in the diet (p 668) by the use of fibrous fruits instead of fruit juices and by the addition of leafy vegetables salads and unmilled grains Bulk is also attained by bran agar and Irish moss

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efficacy of these colossal doses is often observed during diagnostic roentgenography Not infrequently patients report relief of symptoms after the investigation Huge doses however produce a certain amount of intestinal stasis and may even lead to fecal impaction When it is considered that the usual protective powder of *barium bismuth* or *cerium* contains a maximum of a gram of the heavy metal their limited efficiency is better appreciated

Protective action also is obtained from the use of the emollients such as mineral oil from gastric mucin and demulcent colloids such as aluminum hydroxide described in the chapter devoted to therapeutics of the stomach (p 1750)

Intestinal Ferments—Pancreatic ferments are official in the U S P Like gastric pepsin pancreatin is pharmacologically active and therapeutically feeble Except in far advanced pathologic conditions adequate amounts of pancreatic ferment are present in the intestinal tract

Bile Bile Salts and Bile Acids—Normal bile is composed chiefly of *bile salts bile pigments cholesterol* and *lecithin* The bile salts alone are pharmacologically active They are chemically related to estrogen androgen the hormone of the adrenal cortex vitamin D and cholesterol

The official bile preparation is *Ox Bile (Fel Bovis)* U.S P There are three N N R bile preparations *Glycotauro* is a concentrate of ox bile freed from bile pigment and containing approximately 50 per cent of the natural bile salts *decholin* and *decholin sodium* represent the natural bile salts freed from other biliary constituents

In the intestines bile aids the normal digestion of fat and the absorption of fatty acids it emulsifies fat and activates pancreatic lipase Bile salts are essential for the optimum absorption of the fat soluble vitamins A D and K as well as carotene The antiputrefactive action of bile is quite dubious The most important pharmacological uses are stimulation of the flow of bile (cholagogues) catharsis and assistance in vitamin absorption in patients who have *external biliary fistulas* or *obstructive jaundice* (p 1953)

Laxatives and Cathartics—Laxative and cathartic drugs are almost universally employed Their uncontrolled administration is more apt to be harmful than beneficial Milder cathartics are designated *laxatives purgatives* and *drastics* are of increased potency

The Mechanisms of Catharsis—Catharsis may be affected by one of three basic mechanisms The emollients (p 1895) lubricate the intestinal tract they possess no pharmacological action are not absorbed have no toxicity are not habit forming and should be employed before any irritant cathartic measure is advised Their main disadvantage is the tendency to leak through the anal sphincter producing soiling particularly if taken in overdo age by patients with an imperfect or weak shut off muscle

Bulky preparations are employed to increase the content of the intestinal tract they are usually hydrophilic colloids such as the indigestible fiber of the bulky fruits and vegetables they are recommended to individuals who ingest a *low residue diet* (p 668) and those who have atony of the bowel They may produce considerable discomfort in patients with spastic constipation The bulk cathartics are not absorbed they have no toxic action and are not habit forming Occasionally they form gelatinous

Bran which contains almost 20 per cent of undigestible cellulose may be added to cereals and bread

Agar or Agar agar U.S.P is a dried mucilaginous substance obtained from algae It is rich in indigestible hemicellulose When agar is moistened it swells to form a mucilaginous mass Agar may be prescribed in shredded or powdered forms it may be emulsified in mineral oil or desiccated and sold in fine granules

The desiccated granulates are swallowed dry and washed down with water Individuals with cardiospasm or esophageal stricture may develop obstructive symptoms when the hydrophilic action occurs in the gullet and mechanical removal through the esophagoscope may be necessitated Rarely a *fecal impaction* (p 1875) is produced by the swollen agar granules

Most commercial and proprietary preparations sold as Health Foods are essentially granulated desiccated agar, to which laxative such as cascara or phenolphthalein has been added

Irish moss is similar in action to agar the dose of most preparations varies from 10 to 40 gm

Psyllium Seeds—Mechanically irritant substances are added to the intestinal content with the idea of stimulating peristalsis Many health foods' employ irritants as principal ingredients The official irritant is the *Psyllium Seed N.F* taken in a dose of 4 to 15 gm one to three times daily The seeds are washed down by a generous drink of water An esophageal bolus or an impacted fecalith (p 1875) may result from excessive or prolonged use of psyllium seeds When an impaction is suspected the examining finger palpates the offending mass of seed in the lower rectum excavation of the bolus is an arduous procedure and anesthesia may be required

Acidophilus Milk and Cultures—The bacteriological flora of the stool may be altered for therapeutic purposes Normally adult stool is predominantly gram negative due to the presence of colon bacilli Children on a milk diet have a gram positive flora as the result of overgrowth of the colon bacillus by the acidophilus organism

Many experienced clinicians believe that a predominant gram negative flora may give rise to *auto intoxication* and that alteration of the flora to gram positive alleviates symptoms and corrects constipation To achieve this end live cultures of acidophilus organisms suspended in milk or tomato juice are given with the diet The viability of the acidophilus organism is insured by the simultaneous administration of either *lactose* or *betalactose*

To seed the acidophilus organism well the patient takes a quart of acidophilus milk in twenty four hours two to four teaspoonfuls of milk sugar are added to each glass On succeeding days the normal diet is resumed with the ingestion of one pint of acidophilus milk for the daily ration

Protectives—It is difficult to conceive of adequate protection being afforded by drugs to the vast mucous surface of the intestines and colon The amount of the protective substance must necessarily be limited except for the large amounts of barium mixture ingested in the performance of the gastro intestinal radiography (60 to 100 gm suspended in water) The

podophyllum *Jalap* is official as the compound powder the dose of which is 2 gm (30 grains) *Colocynth N F* is prescribed in the dose of 0 125 gm (2 grains) *Elaterin* may be used in the dose of 3 mg (1/20 grain) These drugs are combined in the *Vegetable Cathartic Pill* The dose of the *Resin of Podophyllum U.S.P* is 5 mg (1/12 grain)

The use of any of the resins may lead to watery diarrhea with intense griping and prostration cramps may be so severe as to cause syncope

Castor Oil—Castor oil is obtained from the seed of *Ricinus communis* It is a bland oily substance employed locally on the skin or the mucous surfaces for its soothing properties In the intestines the oil is hydrolyzed to form *ricinoleic acid* a marked irritant which stimulates the motor activity in the small bowel producing copious evacuations within a few hours after administration

The average dose of castor oil is 15 to 30 cc The taste of the oil has been effectively disguised in *Aromatic Castor Oil N.F* and *Emulsion of Castor Oil N.N.R* The use of large elastic globules containing castor oil is not recommended It is difficult to get an adequate dose even with the ingestion of several of these capsules which may stick in the esophagus and have to be removed instrumentally

The purgative action of castor oil is complete and at times depleting The drug should never be employed without the knowledge or prescription of the physician if it is given while the appendix or intestines are inflamed the violence of the catharsis may lead to perforation peritonitis and death

So great is the severity of the effect of castor oil that there is often a succeeding *atony of the bowel* resulting in distention and constipation for the succeeding twenty four to thirty six hours It is for this reason that the castor oil purge has fallen into disfavor in the treatment of acute inflammatory diseases such as lobar pneumonia and as a preoperative routine The latter custom undoubtedly resulted in considerable postoperative intestinal ileus

Castor oil is widely employed by the laity as an *abortifacient* though there is no pharmacologic justification for this use Many obstetricians employ a castor oil purge to *initiate labor* despite the weight of their authority and experience this practice seems unwise and unnecessarily exhausting and depleting The castor oil purge is employed by urologists in the treatment of *pyelitis* particularly in the female It is thought that cleansing of the bowel may influence favorably a *B coli* infection

Croton Oil—Croton oil is the most drastic of all cathartics It is mentioned only to be condemned The dose is one or two drops on a lump of sugar It is said to be the important ingredient of the bartender s Micky Finn administered to get rid of obnoxious barflies

Phenolphthalein—Phenolphthalein is an odorless tasteless powder It is the common ingredient of most *candy cathartics* prescribed in the form of *confections* or *chewing gums* The official adult dose is 0 12 to 0.2 gm (2 to 3 grains) administered preferably at bedtime in order to produce a morning evacuation The effective stool is usually soft and rarely accompanied by colic or distress Phenolphthalein is absorbed in the intestines and may be eliminated by the kidneys producing a red color with an alkaline urine The patient should be warned of this lest he interpret it as

masses which produce an intestinal obstruction or a fecal impaction The bulky cathartic may be used in conjunction with the emollient agent

Active cathartics vary in the degree of irritation but all are dependent for their action upon the production of increased vascularity increased mucus secretion or increased motor activity of the bowels They are potentially toxic are usually habit forming and may induce chronic inflammatory changes The practitioner should discourage their use in so far as possible and should employ them only when simpler methods have failed to produce satisfactory evacuation

Emodin or Anthracene Cathartics—The emodin or anthracene groups of cathartics are plant derivatives which act by virtue of a mild irritation of colon and rectum Their action is delayed for effective morning evacuation they are taken after dinner or at bedtime They may impart a reddish or violet color to the urine and may also cause *melanotic pigmentation* of the rectal mucosa They are excreted in the milk and must not be used during *lactation*

Cascara Sagrada is the most popular of the emodin group The official preparations are the *extract* usually prescribed in pill or tablet form in the dose of 0 3 gm *aromatic fluid extract* the dose of which is approximately 4 cc and *simple fluid extract* given in 2 cc dosage The laxative action of the cascara preparations is usually mild rarely is there any discomfort or griping Fluid preparations have the advantage that the dose may be individually regulated

Senna is widely used by the laity the crude *leaves* or *pods* may be purchased inexpensively and a *decoction* is prepared by permitting the crude drug to soak in cold water for several hours A *tea* is improvised by adding boiling water to leaves or pods The official *Fluid Extract* of Senna is prescribed in 2 cc dosage Many of the laxative nostrums as well as the *Compound Licorice Powder* contain senna as the most important ingredient The action of senna is similar to cascara but is more violent and more apt to cause griping

Rhubarb is rarely used alone except by the pediatrician The *Aromatic Syrup of Rhubarb U.S.P* and the popular *Rhubarb and Soda combination* (the official *Compound Mixture of Rhubarb N F*) are too feeble to be effective in adults A dose of 4 cc may be employed for infants and children In adults and older children the Rhubarb and Soda mixture is fortified with *Fluid Extract of Cascara* Rhubarb preparations contain tannin which has an astringent action that may give rise to a later constipation

Aloe is the most drastic of the emodin group its active principle is *aloin* a glucoside the official preparations are *Aloe U.S P* and *Aloin U.S.P* prescribed in dosages of 0 25 gm (4 grains) and 15 mg (¼ grain) respectively Catharsis from the aloes group may be accompanied by considerable griping This has led to the thoroughly irrational pill of *Aloin Strychnine and Belladonna N F* in which strychnine is present in ineffectual dosage and the belladonna action would have terminated long before the griping of the aloin had been initiated Aloin is the most important ingredient of the official *Compound Laxative Pill N.F*

Resins—The cathartic resins are so intensely irritant that they should rarely if ever be prescribed They include jalap colocynth elaterin and

was commonly 0.3 to 1.0 gm (5 to 15 grains) Most physicians prescribe calomel in a single dose to be taken at bedtime but in earlier days the dose was divided into 10 or 15 parts each portion being taken at ten minute intervals so that the final accomplishment of the total dose was a protracted process

It has also been suggested that the simultaneous administration of bicarbonate of soda decreases the toxicity or irritation of the calomel and increases its efficacy This is exceedingly doubtful and few clinicians employ bicarbonate of soda with calomel All agree however that a *saline purge* is to be administered five to eight hours after the calomel dose The cathartic action of calomel is seemingly due to the liberation of the mercuric ions which irritate the intestinal tract Neither *cholagogue* nor biliary antiseptic activity has been demonstrated

Pharmacological evidence to the contrary most clinicians agree as the result of experience that calomel has some unknown effect beyond the mere mechanical production of defecation It is particularly beneficial in plethoric individuals who are rich livers and heavy drinkers Many abstemious patients who suffer from migraine pseudomigraine intestinal intoxication or biliousness testify to specific relief from a calomel purge

A certain amount of the mercury is absorbed and then excreted in the urine which may reveal albumin and casts Sufficient renal irritation may be produced to cause an effectual diuresis as from the use of the more recently introduced mercurial diuretics (p 2261) In fact the Guy s Hospital Pill contained as its important ingredients digitalis squill and calomel The renal irritation from calomel is not sufficient to justify its contraindication in the nephritic

Those individuals who respond favorably and seemingly specifically to a calomel catharsis should be encouraged to take a prophylactic dose every second or fourth week

Glycerin Suppository—Rectal insertion of a glycerin suppository is a simple method of producing a satisfactory evacuation A considerable proportion of the constipated population suffers because of loss of sensitivity of the defecation reflex (rectal constipation) Under these circumstances rather than employ a drug that will exert its action throughout many feet of the gut the introduction of a glycerin suppository is preferable and most satisfactory

Intestinal Antiseptics and Disinfectants—Until the present day intestinal antisepsis and disinfection have been hopes rather than satisfactory accomplishments Calomel salol and certain of the dyes enjoyed unproved reputations for their efficacy in destroying bacterial invaders of the intestinal tract and contents

The first real progress in this field followed the introduction of *sulfaguanidine sulfathalidine* and *sulfasuxidine* which are elsewhere discussed (p 100) These effectively sterilize the bowel and may be used for prophylactic or curative anti infective therapy

Anthelmintic —See p 1898

SURGERY OF THE SMALL BOWEL

Small intestine and colon are portions of a continuous tube that extends from stomach to anus Most surgical lesions cause mechanical or functional

hematuria An enema administered to a patient taking the drug may be colored red and may mistakenly be interpreted as resulting from a hemorrhagic lesion

Many individuals exhibit curious sensitivity to phenolphthalein A generalized *rash* of the fixed variety may be produced as well as irritation of the *conjunctiva* Upon questioning the patient may deny the use of the drug since it may be taken inadvertently in candy or chewing gum medication or incorporated in an agar preparation

Saline Cathartics—The common saline cathartics include

Sodium Bicarbonate U S P 4 to 15 gm
Magnesium Sulfate (Epsom Salts U S P) 15 gm
Effervescent Salts of Magnesium Sulfate N F 16 gm
Magnesium Magma (Milk of Magnesia) U S P 15 cc
Solution of Magnesium Citrate U S P 200 cc
Magnesium Carbonate U S P 8 gm
Sodium Sulfate (Glauber s Salt) U.S P 15 gm
Sodium Phosphate U S P 4 to 8 gm
Effervescent Sodium Phosphate U S P 10 gm
Potassium and Sodium Tartrate (Rochelle Salts) U S P 10 gm
Compound Effervescing Powder U S P (Seidlitz Powder)—the contents of the blue and white paper dissolved in a glass of water

In addition to official preparations many bottled cathartic and laxative waters are sold by the spas These contain saline preparations in combination None has any particular advantage over the effectual dose of a single saline cathartic

The mechanism of saline catharsis is based on the slow absorption of certain anions and cations notably magnesium sulfate phosphate tartrate and citrate These are retained in the gastro intestinal tract for a relatively long period of time To render them isotonic large volumes of water are ingested to prevent withdrawal of tissue fluid The volume of water exerts a mechanical stimulus increasing motor activity of the intestine The cathartic action is rapid particularly if copious amounts of warm fluids are imbibed with or immediately following the dose.

The ingestion of *concentrated saline solution* may produce an intense *gastritis* and *enteritis* It is bad practice to employ preparations that are not isotonic Obese patients *frequently employ* saline catharsis *for weight* reduction, nothing could be more futile

Saline cathartics are best taken upon awakening The fluids of the breakfast commonly encourage a fluid evacuation shortly following the meal The great advantage of saline catharsis is rapidity of action Many who suffer from *migraine* (p 1506) and *intestinal intoxication* abort or rapidly alleviate symptoms by the timely use of a saline purge

Sulfur—*There is little justification for the use of sulfur as a* cathartic The foul odor imparted to the evacuation is sufficient reason for abandoning the use of these preparations

Mercurous Chloride (Calomel)—Despite its diminishing popularity calomel is one of the most valuable cathartic drugs The methods of administration and doses vary widely Most clinicians employ the drug in the amount of 0 06 to 0 12 gm (1 to 2 grains) In olden times the dose

and dangerous that entero-anastomosis is performed The operative risk is diminished by antibiotic therapy using oral insoluble sulfonamide (p 89) and parenteral streptomycin (p 103)

Resection of the Small Bowel—Resection of the small intestine is performed for diverticula neoplastic disease severe inflammatory lesions extensive or multiple traumatic perforations strangulation thrombosis or embolism involving major intestinal vascular channels The risk depends upon the duration of associated complications such as intestinal obstruction dehydration shock and peritonitis In uncomplicated cases the hazard is slight

The operation of resection consists of excision of bowel and a V shaped segment of mesentery The cut ends of the gut are inverted and closed with two or three layers of sutures An anastomosis is made through a new incision on the antemesenteric side of the bowel This procedure of *side to side entero enterostomy* is preferred to the *end to end anastomosis* Since the lumen is larger there is less chance for obstruction at the site of anastomosis and the blood supply to the sutured area is less apt to be compromised

The risk in surgery of the small intestine is usually considerable since most operative procedures must be undertaken as emergency procedures on gravely ill patients Enterostomy or enterocolostomy on patients in good condition has a mortality of about 2 to 5 per cent Anti infective treatment is given by the combination of oral insoluble sulfonamide (p 89) and parenteral streptomycin (p 103) and penicillin (p 106)

Special Preoperative and Postoperative Care in Small Bowel Surgery.—In an emergency particular care is taken *preoperatively* to assure adequate hydration by means of parenteral fluid administration Shock is combated with plasma or whole blood transfusion During the preliminary waiting period upper intestinal content is aspirated by an indwelling Levine or Miller Abbott tube (p 1823) with constant suction

In intestinal operations of election the patient is prepared with a low residue diet (p 668) for two or three days A Miller Abbott tube is introduced well into the small bowel as near to the level of the lesion as possible This serves postoperatively as an enterostomy and prevents distention of the intestine in the region of any suture line Sterilization of the intestinal content is accomplished by the administration of insoluble sulfonamides such as sulfathalidine (p 101) and oral doses of streptomycin (p 104) Following operation antibiotic treatment is continued with parenteral streptomycin (p 103) and penicillin (p 106)

Postoperatively the patients usually develop *adynamic ileus* (p 4010) for at least three to four days The Levine or Miller Abbott tube is left in place for this length of time and constant suction is applied Small sips of fluid are taken by mouth as long as the tube is functioning well After three or four days the tube is clamped off periodically and reaspirated When the intake of fluid exceeds the quantity aspirated the tube is removed Water balance is maintained during this period by the intravenous drip cathartics neostigmine and pitressin are avoided for at least seven days after operation lest the suture line be disrupted by violent peristaltic movement For special postoperative diets see pp 687–688

obstruction of a portion of the tube Surgical treatment must preserve the continuity of the passage or else provide an artificial opening

Nonpenetrating Procedures—In instances of rare good fortune an intestinal obstruction is discovered to be due to adhesions incarcerations twists invaginations or kinks which can be remedied without the need for incision of the bowel

Enterorrhaphy—Enterorrhaphy involves suture of a perforation of the small intestine The defect may result from trauma such as a gunshot or stab wound or from a disease process such as the perforation of a typhoid ulcer

The operative procedure is simple the risk depends upon the nature extent and duration of the associated infection and the amount of leakage of intestinal content that has occurred into the peritoneal cavity The use of insoluble sulfonamides (p 89) and of parenteral injections of streptomycin (p 103) and penicillin (p 106) greatly reduces the incidence of secondary infection

Enterotomy and Enterorrhaphy—Enterotomy involves incision of the small bowel for the removal of an obstruction due to a foreign body or a benign tumor The operative risk is diminished by antibiotic therapy using oral insoluble sulfonamide (p 89) and parenteral streptomycin (p 103)

Enterostomy—Enterostomy consists of the introduction of a drainage or feeding tube directly into the lumen of the intestine In major resections of the stomach a *feeding enterostomy* is performed in the upper jejunum (*jejunostomy*) to minimize the strain and tension upon the newly made suture line The operative risk is diminished by antibiotic therapy *using oral insoluble sulfonamide (p 89) and parenteral streptomycin (p* 103)

Temporary Enterostomy—In resections of the small intestine temporary enterostomy is performed above the level of resection to short circuit the intestinal current The newly sutured area of bowel is placed at rest thereby minimizing the risk of leakage and favoring healing Temporary enterostomy is also performed in obstruction of the small bowel when the patient s condition is too poor to permit more complete operation Under such circumstances it is an emergency procedure which usually is followed by a more definitive operation when the patient s condition improves

Permanent Enterostomy—Permanent enterostomy is performed in the treatment of extensive ulcerative colitis involving the distal portion of the large bowel and rectum an opening is made in the terminal ileum (*ileostomy*) and the intestinal current is diverted to rest the large bowel and permit the ulcerative lesions to heal As with intestinal resection the risk varies with the patient s condition and the nature of the coexisting intra abdominal complications

Entero anastomosis—Entero anastomosis without resection is performed when obstructed or diseased loops of intestine require short circuiting For example in regional enteritis involving the terminal ileum the ileum above the site of the disease is anastomosed to the transverse colon in order to sidetrack the diseased segment of bowel with extensive intra abdominal *adhesions* associated with chronic or recurrent acute or subacute intestinal obstruction the freeing of multiple adhesions may be so time consuming

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Surgery of the Large Bowel

Surgery of the large bowel presents problems that differ from those encountered in the small intestine

1 The colon acts as a reservoir for intestinal contents so that obstruction produces symptoms more slowly beyond the transverse colon obstruction can be tolerated for four or five days
2 Colonic content, distal to the transverse colon is semi solid in consistency so that permanent ostomies do not necessarily discharge *continuously They can be so constructed that evacuation* takes place once every twenty four to forty eight hours
3 Whereas normally the small bowel is empty four to six hours after feeding the colon always contains virulent bacteria Perforations are therefore much more serious than in the small bowel
4 The wall of the colon is thinner than that of the small bowel its blood supply is more precarious healing is slower and anastomoses are *more prone to leak*
5 Intubation is of less value in colonic disturbances than in those of the small intestine The passage of the tube is stopped at the ileocecal valve so that the obstructed large bowel cannot be decompressed

Special Preoperative Care in Surgery of the Large Bowel and Appendix—In *emergency surgery* of the colon as with perforation and acute obstruction preoperative preparations include the restoration of a normal fluid balance measures aimed at combating shock and efforts to prevent secondary infection by the use of sulfonamides streptomycin and penicillin The patient is given a continuous intravenous infusion plasma is added and antibiotics are injected using penicillin streptomycin and/or sulfonamide The local use of sulfonamide at the operative site may be considered

Procedures are limited to minimal necessary manipulation required to *tide the patient over the emergency More extensive colonic* surgery can then be executed at a later time after adequate prophylactic measures have been more throughly carried out

In *deferred colonic surgery* the patient is prepared by several days of low residue diet (p 668) Enemas and colon irrigations are given daily for two or three days preceding operation until the returns are clear Meanwhile the content of the bowel is sterilized by the administration of one of the insoluble sulfonamides such as *sulfaguanidine sulfasuxidine* or *sulfathalidine* (p 100) or by streptomycin (p 104)

If a proximal colostomy has been previously established as a first stage procedure the colon is washed out both from above and below for several days preceding the more extensive operation The patient s general condition is fortified by transfusion and the liberal administration of vitamins

If an obstructive resection or ileocolonic anastomosis is to be performed the Miller Abbott tube is passed twenty four hours before operation so that it advances *into the terminal ileum*

Nonpenetrating Procedures Involving the Large Bowel—Obstruction of the large bowel may be relieved without incision of the wall in certain instances of *volvulus* (p 1875) *incarcerated hernia* (p 1880) and *intussusception* (p 1876) provided the involved segment of gut is viable

Division of Adhesions —Congenital bands and adhesions resulting from a previous peritonitis occasionally produce *intestinal obstruction* (p 1873) The only necessary procedure may be division of bands provided that the involved segment of gut is viable

Colorrhaphy —Colorrhaphy or suture of a penetration or perforation of the large bowel is a technically simple procedure performed for stab or gunshot wounds and lacerations by foreign bodies or instrumentation The risk is the inevitable peritonitis (p 1923) now more readily prevented and controlled by the antibiotics streptomycin (p 104) and penicillin (p 106) Topical application of sulfonamide also may be considered Perforations of more than twelve hours duration previously were fatal

Colotomy and Colorrhaphy —*Colotomy* consists of opening the bowel to remove a polyp a pedunculated tumor or a foreign body It is followed by suture and antibiotic therapy as for colorrhaphy

Colostomy —The establishment of a colostomy *or artificial anus* is a frequent surgical procedure The stoma provides drainage and external *diversion of colonic content A colostomy is required in most resections* (p 3093) of the large bowel for malignant disease The procedure is also utilized in the chronic types of colitis in order to rest inflamed bowel Occasionally colostomy followed by resection is an isolated procedure for the removal of a benign tumor or polyp

The use of a colostomy for the artificial anus may be temporary or permanent *temporary colostomy* is the initial stage in operable tumors or remediable obstruction later the responsible lesion is attacked at a second stage *Permanent colostomy* is necessitated in operable conditions and resections that require complete closure of the anus the procedure is palliative in inoperable conditions which produce obstruction

The cecum usually is chosen as the site of the colostomy The cecostomy does not interfere with contemplated secondary curative operations Exceptionally with sigmoid or rectosigmoid neoplasms a transverse colostomy is made

Colostomy is performed under local anesthesia The bowel is delivered into the wound and sutured in place In early obstructions the bowel need not be opened for twenty four to forty eight hours thus permitting the peritoneal cavity to become sealed off avoiding contamination In later obstructions the bowel must be opened *immediately* and a large caliber tube sewed in place In this as in other procedures that involve an opening of the lumen of the bowel the gut is sterilized by preoperative use of an insoluble sulfonamide (p 101) or by streptomycin (p 104) Locally the operative site may be dusted with sulfanilamide powder Penicillin (p 106) may be *given with streptomycin (p 101) for inclusive antibiotic* therapy

Following operation the patient is given fluids by intravenous drip Nothing is taken by mouth other than small sips of water until the colostomy begins to function After five to seven days the colon is irrigated through *the anus and the colostomy openings so that inspissated feces is* removed

The risk of colostomy in itself is negligible the patient risk however may be considerable

SURGERY OF THE LARGE BOWEL

Surgery of the large bowel presents problems that differ from those encountered in the small intestine

1 The colon acts as a reservoir for intestinal contents so that obstruction produces symptoms more slowly beyond the transverse colon obstruction can be tolerated for four or five days
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and the procedure is performed in several stages If the entire bowel from cecum to anus is involved in the ulcerative process permanent ileostomy must be established as a preliminary to removal of the colon The operation requires meticulous preoperative and postoperative care

When the anus and distal portion of rectum are uninvolved by ulceration terminal ileum may be anastomosed to rectum or sigmoid This procedure obviates the necessity for performing a terminal ileostomy and permits the bowel to be evacuated normally through the anus Regardless of whether permanent ileostomy or anastomosis between terminal ileum and rectum or sigmoid is performed the actual removal of the colon is usually performed in two or three stages The first stage consists in removal of cecum and ascending and right half of transverse colon After a period of weeks or months the distal portions of the colon are removed

The operative risk is great not only because the patient is often in poor general physical condition but also because the bowel is extremely *friable* Not infrequently as the result of perforations of the bowel localized pericolonic abscesses are present which render surgery difficult and *dangerous* In the hands of the more experienced surgeons the *mortality* in total resections of the colon is no higher than 15 per cent

Appendectomy—See p 1885

Postoperative Care in Surgery of Colon—Following any operation in which there has been an *intestinal anastomosis* for an obstructive resection the patient is forbidden to take anything but sips of fluid by mouth for two or three days If a Miller Abbott tube has been passed before operation fluids may be permitted by mouth in moderate quantities The amount of fluid is gradually increased as tolerated until the clamps are removed from the obstructed loop or there is passage by rectum of stool demonstrating the patency of the anastomosis The diet is rapidly increased to normal intake in twenty four to forty eight hours If the patient begins to vomit a Levine tube is introduced for constant aspiration

Pulmonary complications peritonitis and wound disruption are more common after *colonic surgery* than after most surgical operations The patient must be carefully observed during the early postoperative period for early detection of these disturbances and the institution of appropriate treatment For postoperative colonic diets see p 688

Following *abdominoperineal resection* there is always marked difficulty in micturition because of the interference with the nerves of the bladder For this reason and also because it acts as a guide during operation a catheter is usually introduced before operation and kept in place This should be left indwelling after operation for about six to ten days or longer until spontaneous micturition begins

Loop colostomies and *cecostomies* are frequently not opened until twenty four to seventy two hours after operation The opening is made at this time when the wound has become sealed off from possible fecal contamination The bowel can be opened in its longitudinal axis with a loop cautery There is usually an immediate escape of gas but feces may not pass for twelve to twenty four hours The escaping gas relieves abdominal distention

If there has been anastomosis *enemas* should not be administered for at least eight days after operation and then only cautiously Distention

Partial Colectomy (Resection of the Large Bowel)—Resections of the large bowel differ technically in different portions of the colon In procedures involving a benign lesion such as an obstruction from adhesions volvulus intussusception strangulation or incarceration of a hernia a *temporary colostomy* is first established and the involved segment of bowel is *exteriorized* after division of the mesentery Subsequently the continuity of the bowel is reestablished by an *extraperitoneal anastomosis*

Resection of the bowel in *benign obstruction* may carry a surgical risk as high as 30 to 40 per cent This is partially dependent upon the local surgical complications such as infection and partially on the patient risk (p 1000) The risk varies with the duration of obstruction and the extent of the nonviable bowel

In many *carcinomatous* resections the involved segments of bowel including a generous margin of normal tissue and the supporting mesentery must be removed Operative risk in uncomplicated cases is about 10 per cent If operation is successful there is about a 50 per cent chance for cure A temporary colostomy is performed during the first stage Antibiotic therapy is conducted preoperatively (p 1834) and postoperatively (p 1835) as described

Obstructive Resection—Primary resection with anastomosis is attended with considerable risk of peritonitis from leakage at the suture line In an attempt to obviate this danger the obstructive resection or one of its modifications is performed This procedure is carried out in a number of stages and is applicable only to lesions in the transverse descending or sigmoid colon especially the latter

The *first stage* consists in widely mobilizing the tumor bearing portion of the bowel and bringing the segment out upon the abdomen through the operative incision Large clamps are then applied to the bowel well above and below the tumor The tumor bearing portion of the bowel is then removed between the clamps The clamped proximal and distal segments of the bowel are loosely sutured parallel to one another for a distance of about 4 inches to form the so called *double barreled colostomy* The wound is closed about the two projecting ends of the intestine which are secured by clamps These clamps are permitted to remain in place for a period of about four or five days during which time the peritoneal cavity becomes well sealed off by adhesions When this has occurred the clamps are removed from the ends of the bowel with safety

During the four or five day period in which the bowel is clamped off a mechanical obstruction of the bowel exists hence the name obstructive resection After the clamps have been removed from the ends of the bowel the upper or active segment begins to drain intestinal contents *At the end of seven to ten days a special type of spur crushing clamp* is applied to the two loops of bowel in such a manner that their opposed walls are cut through Following the crushing of the spur the major portion of the intestinal contents from the upper loop passes into the lower loop without being discharged upon the surface of the abdomen The *final stage* of the procedure consists in closing the stumps of the bowel for the reestablishment of continuity

Complete Colectomy—*Complete colectomy is performed in* ulcerative colitis involving the major portion of the large intestine Patients who require complete colectomy are usually in poor general physical condition

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In many *carcinomatous* resections the involved segments of bowel including a generous margin of normal tissue and the supporting mesentery must be removed Operative risk in uncomplicated cases is about 10 per cent If operation is successful there is about a 50 per cent chance for cure A temporary colostomy is performed during the first stage Antibiotic therapy is conducted preoperatively (p 1834) and postoperatively (p 1835) as described

Obstructive Resection —Primary resection with anastomosis is attended with considerable risk of peritonitis from leakage at the suture line In an attempt to obviate this danger the obstructive resection or one of its modifications is performed This procedure is carried out in a number of stages and is applicable only to lesions in the transverse descending or sigmoid colon especially the latter

The *first stage* consists in widely mobilizing the tumor bearing portion of the bowel and bringing the segment out upon the abdomen through the operative incision Large clamps are then applied to the bowel well above and below the tumor The tumor bearing portion of the bowel is then removed between the clamps The clamped proximal and distal segments of the bowel are loosely sutured parallel to one another for a distance of about 4 inches to form the so called *double barreled colostomy* The wound is closed about the two projecting ends of the intestine which are secured by clamps These clamps are permitted to remain in place for a period of about four or five days during which time the peritoneal cavity becomes well sealed off by adhesions When this has occurred the clamps are removed from the ends of the bowel with safety

During the four or five day period in which the bowel is clamped off a mechanical obstruction of the bowel exists hence the name obstructive resection After the clamps have been removed from the ends of the bowel the upper or active segment begins to drain intestinal contents At the end of seven to ten days a special type of *spur crushing clamp* is applied to the two loops of bowel in such a manner that their opposed walls are cut through Following the crushing of the spur the major portion of the intestinal contents from the upper loop passes into the lower loop without being discharged upon the surface of the abdomen The *final stage* of the procedure consists in closing the stumps of the bowel for the reestablishment of continuity

Complete Colectomy —Complete colectomy is performed in ulcerative colitis involving the major portion of the large intestine Patients who require complete colectomy are usually in poor general physical condition

CHAPTER 92

CLINICAL DISTURBANCES OF THE INTESTINES LOCAL MANIFESTATIONS OF SYSTEMIC DISORDERS

The small and large intestines exhibit local manifestations of widespread systemic disorders of metabolic vascular neurogenic and infectious origins

METABOLIC DISTURBANCES

ENTERITIS DUE TO VITAMIN B DEFICIENCY

Intestinal disturbances are often associated with deficiencies of the various moieties of the *vitamin B complex* (p 622) The fundamental abnormality may be a failure of adequate absorption or a dietary deficiency

Clinical Manifestations —The presenting symptoms include *anorexia weakness* and *paresthesias* involving the extremities Often there is a persistent and intractable *diarrhea* of apparently unknown etiology

The examinations reveal *abdominal distention* an *anemia* of the primary or secondary type normal or absence of acidity in the gastric contents and often an *excess of fat* in the stool

Roentgenograms of the small bowel reveal a peculiar variation in the caliber of the intestinal loops The contrast meal gives the *impression of a puddling* in certain dilated loops while others appear to be narrowed In addition the normal pattern of the mucous membrane is obliterated and motility is increased It is quite possible that more advanced stages progress to a *primary diffuse polyposis* or *granuloma formation* (p 1865)

Treatment —There is a rapid symptomatic response to the administration of *liver extract* (p 1048) The clinical symptoms disappear and the normal mucous membrane pattern becomes reestablished

THYROGENIC DIARRHEA

A characteristic and frequent accompaniment of *hyperthyroidism* (p 1197) is an *intractable diarrhea* (p 1840) In the early stages the bowel disturbance is rather a polyrrhea in that the bowels move frequently but

may be alleviated by using glycerin or soap suppositories An enema given incautiously can easily rupture a suture line and produce a rapidly fatal peritonitis

In addition to the complications occurring after other types of intra abdominal operations patients with appendicitis occasionally develop temporary *fecal fistulas* due to slipping of the ligature on the appendix stump Frequent dressings are required to keep the wound clean The fistula closes spontaneously unless it is symptomatic of a regional *ileitis* (p 1851)

The preoperative routine of combined antibiotic therapy using oral insoluble sulfonamide (p 89) and parenteral streptomycin (p 103) and penicillin (p 106) is resumed immediately following all operations involving the bowel or appendix and is continued well into convalescence

Infestations	Particularly uncinariasis giardiasis balan tidiasis and trichinosis Examine stools for ova and parasites Note eosinophilia (p 542)
Rectal	False diarrhea with fecal impaction Passage of small quantities of inspissated stool but re tention of larger ma s in ampulla
Pancreatic	Functional or organic pancreatic insufficiency with copious stools containing undig ted fat and muscle fiber Use high protein diet and pancreatic extract (p 1936) Celiac disease of infancy and childhood
Hemic	Macrocytic hyperchromic anemia Note char acteristic hemogram and therapeutic re ponse to liver extract (p 1048)
Special Types in Infancy	Epidemic diarrhea or cholera infantum in early life Celiac disease with pancreatic insuf ficiency Idiosyncrasy to milk or eggs

the action is formed and the quantity is not excessive The stools later become fluid and increased in bulk and weight further adding to the depletion and asthenia of the sufferer *Masked hyperthyroidism* is of suf ficiently frequent occurrence so that in any otherwise unexplained exam ple of diarrhea a basal metabolic rate determination is required (p 3739)

The *treatment* of thyrogenic diarrhea is that of the underlying condi tion (p 1210)

INTESTINAL CRISES IN ADRENAL CORTICAL DEFICIENCY

Gastro intestinal crises characterize the acute exacerbations of *adrenal cortical deficiency* (p 1271) There is no specific lesion The obvious pres ence of the endocrinopathy leaves no doubt as to the origin of the diges tive symptoms which are relieved by *sodium chloride* and/or the active *hormone* (p 1267)

UREMIC COLITIS

Of the *endogenous intoxications* a terminal colitis of toxic origin is ob served not infrequently in *uremia* (p 2276) Treatment is symptomatic

COLITIS DUE TO POISONINGS WITH HEAVY METALS

Exogenous poisonings are very frequently associated with abdominal cramps and diarrhea due to the excretion of the drug through the intes tinal mucous membrane More specifically this is observed in the colic of *plumbism* (p 76?) and the colitis associated with poisonings by *mercury* (p 765) and *arsenic* (p 752) Since the poison may be reabsorbed by the intestinal mucosa *treatment* includes colonic irrigation

ALLERGIC COLITIS

The bowel acts as a sensitized end organ and shock tissue in certain of the allergic disorders (p 547) In all likelihood lesions are produced which resemble the visible dermatoses these may be *urticarial angioneu rotic purpuric* or *erythematous*

The offending allergen may be a *digestant* a *drug* or a *bacterial sub* The most frequently responsible foodstuffs are milk eggs wheat

DIFFERENTIAL DIAGNOSIS OF

Diarrhea

Diarrhea is a symptomatic complaint that may be of intestinal or extradigestive origin It is to be distinguished from polyrrhea in which the individual passes *frequent small stools whose total bulk is not in excess of the single daily passage*

The term diarrhea includes abnormalities in the quantity or character of the stool The passage of frequent mushy or fluid stools indicates an abnormality in evacuation time which requires investigation

	DIAGNOSTIC FEATURES
Hygienic	Gluttony Excessive ingestion of carbonated fluids whether alcoholic or non-alcoholic Edentia Eating unripe foods such as apples which ferment in the intestine Ingestion of putrefactive cheeses
Psychogenic and Psychosomatic	Excitement. Nervous tension Hypersthenic neuroses with mucous colitis Regional ileitis and nonspecific ulcerative colitis Search stools for ova parasites amebae and pathogenic bacteria (p 3727) Get barium meal and enema If all tests are normal consider technical psychotherapy (p 1316)
Pharmacodynamic	*From excessive doses of laxatives and cathartics* particularly of the candy variety With anthelmintics
Poisonings	Particularly mercury arsenic and lead
Metabolic	Vitamin B deficiency particularly pellagra with therapeutic response to thiamine riboflavin and niacin Sprue and pancreatic insufficiency with bulky stools containing undigested fat and muscle fibers Terminal uremia with azotemia Amyloidosis with hepatosplenomegaly and retention of congo red
Allergy	Following ingestion of specific offending substance often fish or pork.
Endocrinopathy	Hyperthyroidism with elevation of B M R. and therapeutic response to iodide Crises of adrenal cortical deficiency with pigmentation asthenia and hypotension
Generalized Infections	Staphylococcic and streptococcic food poisonings Typhoid and paratyphoid (Salmonella) fevers Miliary tuberculosis *Bacillary and* amebic dysenteries Cholera Trichinosis Culture stools for predominant pathogenic organism Examine blood for eosinophilia agglutinin titers and bacteriology (p 59)
Gastric	Achylia gastrica with absence of HCl from gastric analysis Symptomatic relief from administration of acid (p 1754)
Intestinal	Acute nonspecific gastro enteritis Nonspecific acute and chronic colitis Polyposis Amebic dysentery and helminthiasis Tuberculous enterocolitis Localized peritoneal abscesses involving left colon Ulcerating carcinomas of the large bowel Examine stools for occult blood ova parasites amebae and pathogenic bacteria (p 54) Get barium enema, barium meal and sigmoidoscopy (p 1907)

C NUED

13—Consider surgical procedures in intractable diarrhea with progressive weight loss
14—Order vermicides and vermifuges in infestations (p 1891)

DIFFERENTIAL DIAGNOSIS OF

Melena and Tarry Stools

Bleeding into the bowel may result in the passage of tarry burgundy or red streaked stools The tarry stool represents digested blood and must be differentiated from blackening due to the ingestion of bismuth iron, charcoal or spinach Burgundy stools are encountered when bleeding is associated with diarrhea and these must not be confused with the reddening of the water in the bowl noted after the ingestion of beets Red blood streaking suggests that the bleeding has not occurred until the stool has been molded in the recto-sigmoid, hence the site of the hemorrhage should be visible by proctoscopy or sigmoidoscopy (p 1907)

	DIAGNOSTIC FEATURES
Upper Digestive	*Tarry stools from bleeding gums* epistaxis ruptured esophageal varices and ulcerating peptic ulcer or gastric cancer Observe barium meal and perform esophagoscopy or gastroscopy if necessary (p 1745)
Intestinal	In severe types of ileitis or colitis Ulcerations of the bowel in typhoid fever tuberculosis (p 1860) Meckel s diverticulum, diverticulitis intestinal polyposis or malignancy With volvulus and intussusception Examine stools for ova parasites amebae and pathogenic bacteria (p 54) Get barium meal and barium enema *Perform sigmoidoscopy (p 1907)*
Trauma and Chemical Injuries	With impaction of foreign bodies and poisoning with mercury
Helminthiasis	Particularly hook worm disease Note eosinophilia and search stools for ova (p 1894)
Rectal	Fresh red blood in hemorrhoids rupture of perianal abscess ulceration of neoplasm or impaction of foreign body Make digital examination and perform sigmoidoscopy (p 1907)
Generalized Infections	Particularly typhoid and paratyphoid fevers bacillary dysentery amebic dysentery cholera and yellow fever Get blood and stool cultures Note agglutinin titers in serum (p 59)
Circulatory	Following mesenteric and portal vein thrombosis
Hematopoietic	*In thrombocytopenic purpura* vitamin K deficiency (hemorrhagic disease of the newborn) vitamin C deficiency (scurvy) leukemia hemophilia and acute capillary toxicoses (Henoch s purpura) Note hemogram and bleeding and coagulation times Observe cutaneous purpura (p 3423) Try therapeutic responses to cevitamic acid and menadione (p 630)
In the Newborn	With cord infection and vitamin K deficiency (melena neonatorum) Note therapeutic response to menadione (p 630)

strawberries fish pork, shellfish onion chocolate tomato and cabbage Therapeutic substances to which gastro intestinal idiosyncrasy is evinced include the analgesic antipyretics (p 3832), liver extract and cathartics *Bacterial allergy is seen also in the visceral manifestations of the purpuras* (p 3423) the intestinal participation is suggested when there is an asso ciated visible skin lesion as in *anaphylactic purpura* (p 3422) or the digestant urticarias Without the dermatosis the diagnosis rests on the his tory since skin tests may be corroborative absent or misleading

The clinical manifestations of allergic colitis consist of *vomiting ab dominal pain* and *diarrhea* There may be *collapse* in the more severe ex amples *Associated manifestations may include generalized pruritus or pruritus ani* and *headache* an *eosinophilia* may be demonstrable A par ticularly violent type of intestinal allergy is produced by the bite of the black widow spider (p 3197)

Intestinal allergy is treated by the use of *elimination diets* (p 683) Absolute proof of the nature of the condition is established by provoking in attack through deliberate readministration of the offending substance The acute symptoms may be dramatically alleviated by injections of *epinephrine* (p 3877) or by the anti histamine action of pyribenzamine (p 565)

GASTROGENOUS DIARRHEA

Gastrogenous diarrhea occurs with *achylia* (p 1768) The symptoms are often relieved by the administration of *hydrochloric acid* (p 1754)

SYMPTOMATIC TREATMENT OF DIARRHEA

If the causative factor in diarrhea cannot be removed symptomatic measures must be employed

1 —Eliminate dietary errors such as gluttony and the excessive use of carbonated drinks
2 —Stop all laxative and cathartic drugs
3 —Provide dentures for the edentate
4 —Use smooth low residue diet in spasmosis and other *hypersthenic* conditions
5 —Employ high protein diet in pancreatic insufficiencies Use protein milk bananas or banana powder
6 —Administer hydrochloric acid before and during meals in achylia gastrica
7 —Give iodides in thyrotoxicosis and sodium in Addisonian crises
8 —In food poisonings and intestinal infections order frequent small feedings of bland non residue foods such as cocoa boiled rice tea and toast Avoid irritant catharsis particularly with castor oil
9 —Try specific therapy with soluble on insoluble sulfonamides and/or parenteral streptomycin in bacillary dysentery and cholera
10 —Give emetine in amebic diarrhea or in conditions suspected of being amebic
11 —Try heliotherapy and streptomycin in tuberculous enterocolitis
12 —Consider technical psychotherapy in intractable intestinal neuroses and psychosomatic conditions such as regional ileitis and non specific ulcerative colitis

motor and secretory responses which vary with the individual pattern Relaxation is produced by drugs which depress the vagus The adrenergic preparations both the stimulants and the depressants have little clinical significance

Differences Between Gastric and Intestinal Neuroses—There are certain fundamental differences between gastric and intestinal neuroses The hydrochloric acid in the stomach protects against infection and the somatization is expressed by the *erosive peptic ulcer* (p 1780) In the lower bowel where the reaction is alkaline bacterial growth is uninhibited and the irritated mucous membrane becomes secondarily infected so that the *psychosomatic equivalent* is an infectious inflammatory process clinically *identified as regional ileitis* (p 1851) in the small bowel and *nonspecific ulcerative colitis* in the lower bowel These fundamentally neurogenic processes are not to be confused with the primary bacterial invasion such as typhoid fever the dysenteries and tuberculosis

Psychosomatic Intestinal Manifestations—The inclusion of regional ileitis and chronic nonspecific ulcerative colitis in the category of the psychosomatic manifestations will be severely criticized by the organicists Not without justice they will argue that the case is not proved and the evidence altogether too flimsy for acceptance However they cannot deny *the following clinical observations upon which our present attitude depend* (1) Regional ileitis and chronic nonspecific ulcerative colitis occur in the relatively *young* (2) the afflicted give evidences of a preexistent *autonomic imbalance* (3) the onset of symptoms is often associated with *emotional stress* (4) in comparison to those who suffer from other intestinal infections a disproportionately large number of patients are *sexually maladjusted* (5) a specific infectious organism has never been isolated in either of these entities (6) specific treatment has never met with other than sporadic success and (7) the operation of other etiological factors has never been demonstrated (p 1344)

Our present inclusion of these disturbances as somatizations of the intestinal neuroses is admittedly tentative but it fulfils the purpose of directing the attention of the therapist to the *patient as a whole* rather than to his bowel

Reflex Intestinal Neuroses—Reflex intestinal neuroses result from *local disease* of the digestive system notably inflammation and stone formation *in the* gallbladder (p 1997) or ulcerations in the neighborhood of a malignant growth (p 1815) *Remote systemic disturbances* such as gynecological disease renal and ureteral colic and coronary occlusion may also produce reflex intestinal neuroses

The *treatment* of the reflex intestinal neurosis is directed toward the causative mechanism Since the latter may be latent and insidious a meticulous investigation is warranted before concluding that the patient suffers *from the functional intestinal neurosis*

Functional Intestinal Neurosis—The functional intestinal neurosis resembles the gastric neurosis (p 1767) The same predisposing and exciting causes are operative Manifestations of *autonomic imbalance* (p 1395) are demonstrable attesting to the fact that the disturbance is a portion of a more widespread abnormality The clinical picture is never that of a pure vagotonia or a sympathicotonia but is a mixture of both elements

VASCULAR DISTURBANCES

MESENTERIC OCCLUSION

Mesenteric occlusion leading to gangrene of the gut follows closure of the *venous or arterial blood supply* to a segment of the intestines *Venous thromboses* occur in polycythemia vera (p 1093) and with increased portal pressure due to a cirrhosis of the liver (p 1969) *Arterial occlusions* of the mesenteric vessels may result from generalized arteriosclerosis (p 976) or periarteritis nodosa (p 1027) *Embolic closure* occasionally follows an acute coronary *thrombosis or lodgment of an errant vegetation in* subacute bacterial endocarditis (p 1021)

Clinical Manifestations —In each of these instances the acute bowel episode punctuates the course of a chronic illness With a closure of sufficient size to produce gangrene of an appreciable segment of gut the patient suffers an *acute abdominal catastrophe* (p 1748) There is a sudden onset with severe abdominal pain associated with collapse The blood pressure falls The skin is cold and clammy and there are all the clinical evidences of *peripheral shock* (p 928) The abdomen becomes distended There is intractable vomiting elevation of temperature and a leukocytosis The nature of the disturbance is inferential unless the patient passes a stool containing bright red blood Often the diagnosis of a mesenteric thrombosis is an operative finding not previously suspected

Treatment —The treatment of infarction of the small intestine is surgical The operation is delayed to permit the patient to recover from the forward failure that is usually present (p 928) If the loop of the bowel is not viable *resection* (p *1832*) is indicated

HEMORRHAGIC LESIONS

Hemorrhagic and purpuric manifestations involve the bowel as well as the visible skin and mucous membranes In the bleeding diatheses such as *thrombocytopenic purpura* (p 1114) *hemophilia* (p 1118) or *melena neonatorum* (p 2782) a presenting and persistent symptom may be the presence of *blood in the stool* Melena is also seen in *Henoch's purpura* (p 3424)

NEUROGENIC AND PSYCHOSOMATIC DISORDERS

Much of what has been written on the subject of the gastric neuroses (p 1767) applies equally to the neurogenic disturbances that involve the lower bowel The manifestation may be *reflex* or *functional* (p 1767) There are *predisposing factors* (p 1772) in the constitution of the individual the psyche the involuntary nervous system and the end organs The *exciting circumstances* (p 1773) which set off or perpetuate the derangement include emotional stresses dietary indiscretions the use of alcohol and tobacco and the clinical entity known as auto-intoxication

The *symptoms* of the intestinal neurosis may be *hypersthenic* or *hyposthenic* (p 1773) Under circumstances not yet completely understood the functional disturbance may progress to somatization giving rise to the entities of *regional ileitis* (p *1851*) *and chronic nonspecific ulcerative colitis* (p 1856)

The small and large intestines are innervated by the *cholinergic* and *adrenergic systems* The former is the more potent and stimulation evokes

The commonest complaints are abdominal distress discomfort and pain The site of the misery may be generalized with involvement of the entire bowel right sided if cecal and left sided if sigmoidal If the *circular muscle* is primarily involved a spasmosis exists and the patient notes obstinate constipation Hypersthenia of the *longitudinal muscle* leads to hypermotility and the passage of frequent or diarrheal stools An associated *hypermyxorrhea* produces the clinical picture of mucous colitis Often the mucous plaques are mistaken for worms (p 1891)

The physical examination of the patient with intestinal neurosis reveals disproportionately few findings relative to the wealth of subjective complaints Despite the long duration and intensity of the symptoms the patient is well nourished and there are no constitutional accompaniments such as fever tachycardia or leukocytosis The *autonomic imbalance* is revealed by cold clammy extremities and a ready tendency to blushing and blanching Because of the essentially cholinergic character of the disturbance there is often an associated *bradycardia*

In conditions of hypermotility the churning of the intestinal content in the bowel (borborygmi) may be heard and felt In spastic conditions the viscera are palpable most often in the cecal or sigmoidal regions and less frequently in the transverse colon The spastic viscera are palpable as elongated sausage like masses They are often tender when rolled by the examining finger and the patient reports that the painful complaint has been reproduced Often they appear and disappear during examination causing the suspicion of a *phantom tumor* They are frequently felt when the patient has no symptoms related to the local disturbance

Gross examination of the stool affords very characteristic findings In the spastic variety of the neurosis the patient passes round pellets about the size of a marble At other times the stool has the appearance of a hand rolled cigarette about 1½ to 2 inches in length with twirled ends With an increased secretion of mucus there may be a veil over the fecal mass

Laboratory Findings —The laboratory findings are completely normal in the presence of a functional intestinal neurosis The demonstration of pus or red cells in the stool of fever leukocytosis or increase in the sedimentation rate indicates the presence of some organic disease Radiography reveals bizarre patterns in the small bowel and exaggerated haustrations in the large bowel if there is spasmosis but with hypertonicity of the longitudinal muscles the colon is of diminished caliber By sigmoidoscopic investigation hyperplasia of the mucous membrane may be seen and the amount of mucus is increased

Diagnosis —Functional intestinal neurosis is diagnosed only when organic disease can be excluded The infectious and inflammatory conditions are accompanied by constitutional manifestations such as blood and pus in the feces Chronic lesions such as malignant growths of the gut (p 1888) appear later in life and undermine the general well being of the patient radiographic examination discloses filling defects or obstruction and occult blood is revealed in the stool

Course —The course of the intestinal neurosis is characterized by episodes of exacerbation and remission In favorable instances the disturbance abates as the patient grows older A small number of the more

The functional intestinal neurosis requires differentiation from the reflex intestinal neurosis and the somatizations The astute practitioner will insist on positive evidence of morphological integrity before he commits himself to the nonorganic diagnosis Tangible and objective laboratory assistance is of the greatest value in arriving at the decision The hollow bowel should be delineated by the *barium meal* and the *barium enema* *Scout films* are taken with the express purpose of demonstrating calculi in the gallbladder region and the sac is outlined by *cholecystography* (p 2000) The *gastric contents* and the *stool* are examined (p 3728) A *hemogram* (p 3704) is required and an estimation of the *basal metabolic rate* (p 3738) is distinctly in order

Only when he is satisfied that his patient shows no demonstrable evidence of morphological disease does the practitioner commit himself to the diagnosis of the functional intestinal neurosis As a further safeguard the examinations are repeated if the symptoms persist change in quality or intensity or recur with too great frequency

Types of Intestinal Neurosis —Consideration of the intestinal neurosis is simplified by reducing their manifestations to the categories of hypersthenic and hyposthenic varieties The *hypersthenic* variety includes irritable colon mucous colitis spastic constipation spastic sigmoid spastic cecum appendicular colic and intestinal hypermotility The *hyposthenic intestinal* neuroses are fewer in number and embrace the conditions of intestinal atony and paralytic ileus

HYPERSTHENIC INTESTINAL NEUROSES

The hypersthenic neurosis may be *motor* or *secretory* but most often these features are combined The muscular hypertonia may manifest itself by producing *spasm* or by increasing *propulsive movement* The former condition results in the spastic types of constipation while the latter produces frequent bowel motions When the diarrheal variety is accompanied by hypersecretion of intestinal mucus the condition of *mucous colitis* is diagnosed

The hypersthenic condition may be generalized throughout the bowel or localized in the region of the sigmoid the cecum or the small bowel The most difficult clinical manifestations are those in which there is hypermotility in the small intestine and spastic constipation in the colon

Considerable confusion has arisen from the fact that some of these phenomena have been given names and are regarded as clinical entities The concept of an irritable colon mucous colitis spastic constipation 'spastic sigmoid appendicular colic intestinal hypermotility and spastic cecum is decidedly limited and is best discarded by the clinician for the more inclusive perspective of a hypersthenic intestinal neurosis

Clinical Manifestations —The clinical manifestations of the hypersthenic intestinal neurosis are as varied as the facial appearances of those who suffer from this condition As with the gastric neurosis however each patient has a distinctive reaction picture which is reproduced accurately without respect to the nature of the provocative agency Each patient has his personal brand of bellyache which he regards with a curious combination of affection and annoyance

in evacuation and a sense of incomplete emptying Cathartics are taken in increasing dosage Gentle laxatives are used at first and later the drastics are alternated with saline purging Secondary to the bowel inertia the patient complains of abdominal distention flatulence belching the passage of flatus (which may have an offensive odor) headache listlessness anorexia somnolence and irritability The condition of the bowels and the bowel movements constitute the dominant interest and topic of conversation

The patient is colon conscious and usually ends up with a rosette or hemorrhoids from excessive purging and rectal fissures from trauma due to frequent enemas and irrigations On examination there may be a coating of the tongue and a heavy odor to the breath The abdomen appears distended and doughy masses of fecal material may be palpated abdominally and rectally Radiography reveals lazy peristaltic movements

DIFFERENTIAL DIAGNOSIS OF

Swellings and Tumors in the Left Upper Quadrant

Swellings and tumors in the left upper quadrant are infrequently encountered other than splenomegaly Their clarification may necessitate x ray examinations of colon and the upper urinary passages Under any circumstance hematologic studies are included since splenic enlargement is associated so frequently with disorders of the hematopoietic system (p 1131)

	DIAGNOSTIC FEATURES
Splenic	See Splenomegaly (p 1131)
Renal	Ptosis or enlargement of the kidney Confirm findings by urinalysis urography and cystoscopy (p 2248)
Colonic	Spasm or malignancy of splenic flexure Get barium enema (p 1824) and multiple examinations of stool for occult blood (p 3728)
Pancreatic	Cysts or malignancy of tail of pancreas Confirm by exploratory laparotomy

and some delay in the forward progress of the head of the column Areas of the bowel and particularly the rectal ampulla may be considerably dilated

The acute manifestations of the hyposthenic intestinal neurosis are more often toxic in origin and are seen in the course of an acute infectious disease or following operative procedures The clinical manifestations and treatment of *acute gastric dilatation* (p 1807) and *paralytic ileus* (p 1851) are elsewhere discussed

Diagnosis—The hyposthenic intestinal neurosis requires differentiation from obstructive conditions of the bowel most particularly the *annular scirrhous carcinomas* (p 1888) It is only by recourse to the barium meal and the barium enema supplemented by sigmoidoscopic investigation that a differential diagnosis can be established at the time when the organic condition is operable

Treatment—The treatment of hyposthenic intestinal neuroses is quite unsatisfactory *Psychogenic factors* are less successful than in the hyper

seriously afflicted go on to somatization and develop *regional ileitis* (p 1851) or *chronic nonspecific ulcerative colitis* (p 1856)

Treatment —Treatment of hypersthenic intestinal neurosis follows the lines laid down for the management of gastric neuroses (p 1767) *Psychotherapy* (p 1316) is combined with the administration of *sedatives* (p 3636) *hypnotics* (p 3830), and the *cholinergic depressants* An eminently satisfactory arrangement of the drug routine calls for the use of a *belladonna derivative* before meals and *Mistura Nigra* (p 1757) after meals and at bed time a *bland diet* is ordered roughage is avoided as are irritants such as coffee tea alcohol condiments raw and uncooked foods salads and the leafy vegetables *mineral oil* given orally or by rectal instillation at bed time often has a soothing effect laxatives and cathartics are strictly

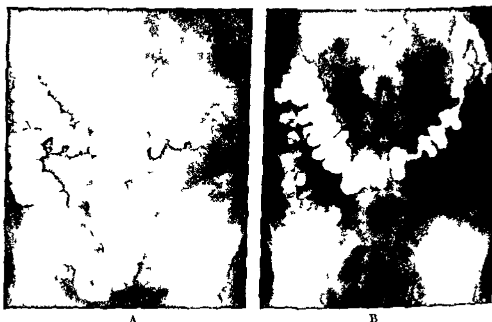


Fig 411 —Spastic constipation *A* Appearance of colon at six hours *B* Appearance at twenty four hours

avoided the application of *heat* to the abdomen is often grateful beyond explanation

Patients who fail to respond to ambulatory treatment are advised to spend a week end in bed or take a modified *rest cure* Those who are in a position to do so gild the infirmity by indulging in hospitalization

HYPOSTHENIC INTESTINAL NEUROSES

Hyposthenic intestinal neuroses are as frequent as the hypersthenic variety but they rarely come to the attention of the practitioner since the patient being free from pain indulges in self medication

Clinical Manifestations —The hyposthenic intestinal neuroses are manifest as conditions of *intestinal atony* which give rise to *constipation* and the symptoms of *auto intoxication* The patient notes increasing difficulty

* Buckstein Clinical Roentgenology of the Alimentary Tract

1—Correct hygiene by giving high residue diet with atonic conditions and smooth diet in spasmosis Order at least 8 glasses of water daily Increase abdominal tone by exercise or walking Encourage regular habits by instructing the patient to sit on the commode after breakfast while reading the morning newspaper

2—With dyschezia and other types of anorectal constipation insert glycerine suppository or take a small rectal flush after breakfast

3—Except under unusual circumstances the enema should be made with tap water or saline Soap suds are as irritant to the rectal mucosa as they are to the eye

4—The use of a corset may be corrective in weakness of the abdominal wall as well as in the elderly and multipara

5—In atonic conditions order 1 or 2 teaspoonfuls of bicarbonate of soda in 2 glasses of hot water 15 minutes before breakfast

6—In acute paralytic ileus prescribe prophylactic and remedial dose *of neostigmine using 0.5 to 1 0 cc intramuscularly unless there* are contra indications

7—Desensitize the patient relative to disgust with the passage of stool and with the unesthetic practices of anal and rectal hygiene (p 1909)

8—For immediate catharsis in acute constipation employ a saline laxative such as the bicarbonate of soda as above sodium phosphate (p 1830) or magnesium sulfate (p 1830)

9—When bulk cannot be supplied adequately in the diet prescribe agar but avoid seeds particularly psyllium which may cause irritation and fecal impaction

10—In spastic constipation when correction of hygiene fails prescribe a high fat diet including butter and olive oil but if this is not successful give additional doses of mineral oil Pharmacotherapy with vagal depressants such as atropine and the newer substitutes in our experience accomplishes nothing useful

11—For patients who have jaundice and definitive biliary disturbances prescribe bile salts (p 1827)

12—Persist with above efforts attempting to avoid the use of laxatives and cathartics Remember that mineral oils remove fat soluble vitamins from the intestinal tract and saline cathartics may be followed the next day by post cathartic constipation and exacerbation of the symptoms of auto intoxication

13—All else failing if constipation cannot be relieved resort to the simpler laxatives such as cascara sagrada or phenolphthalein Except under the most unusual circumstances avoid the drastics such as jalap aloin podophyllum croton oil calomel the sulfur preparations and castor oil

14—Order thyroid extract for those with hypometabolism

REGIONAL ILEITIS (CHRONIC IDIOPATHIC ULCERATIVE ENTERITIS)

Regional ileitis is a rare disease of the small intestines characterized by the formation of nonspecific granulomas Males are affected twice as often

sthenic varieties and *drug therapy* is of less avail The patient is placed on a *roughage diet* (p 668) which may be supplemented by the addition of *agar* (p 1825), *Irish moss* (p 1825) *bran* or *psyllium seeds* (p 1826)

Careless patients are told of the importance of bowel hygiene and are urged to become conditioned to the habit of securing a morning evacuation Simple adjuvant measures include the drinking of one or two glasses of hot water containing a teaspoonful of bicarbonate of soda and the juice of half a lemon on arising and the insertion of a glycerin suppository following breakfast Should these procedures fail, a rectal flush insures a daily cleansing of the lower bowel and is less objectionable than the habitual administration of laxative and cathartic drugs (p 1827)

The patient with the 'cleanliness complex' is reassured that constipation is not too filthy or harmful She is urged to try the simple methods of



Fig 41⁰—Rectal constipation Appearance at seventy two hours

therapy and avoid the continued use of drastics Implants of *acidophilus milk* (p 1826) may be helpful In larger cities patients with intestinal atony indulge enthusiastically in enemas and colon irrigations (p 1824) The latter cater to the anal eroticism of all concerned

In acute atonies intramuscular injection of *neostigmine* and *pitressin* (p 3888) are of invaluable prophylactic and therapeutic value

Symptomatic Treatment of Constipation

The treatment of constipation is essentially aimed at the elimination of the cause The use of laxatives and cathartics is avoided unless other measures fail

Buckstein Clinical Roentgenology of the Alimentary Tract

Peritoneal	Reflex ileus in acute and chronic peritonitis Consider abdominal puncture or laparotomy
Psychogenic	Coprophobia due to fear or disgust Ileus as thema Hysteria Anorexia nervosa Depressive psychoses Hypotonic and hypertonic gastro-intestinal neuroses with atony or spasmosis If stools and x rays are normal advise psychotherapy (p 1316)
Neurogenic	Transverse myelitis hematomyelia spinal cord tumors spinal cord scleroses and tabes dorsalis Supplement neurologic findings with examinations of cerebrospinal fluid (p 3734) In all instances of increased intracranial tension particularly when associated with persistent vomiting In all instances of coma
Pharmacologic	With opiates hematinics containing iron and general anesthetics In plumbism
Generalized Infections	In all febrile disorders associated with anorexia and increased sweating
Circulatory	Backward failure with chronic passive congestion of gastro-intestinal viscera
Endocrinologic	Myxedema with low B M R and therapeutic response to thyroid extract Adrenal cortical deficiency with pigmentation, hypotension and asthenia Anterior pituitary deficiencies resembling anorexia nervosa with low B M R and cachexia
Gynecologic	In early and late pregnancy With uterine malposition rectocele and obstructions due to endometriosis Make careful vaginal examinations (p 3648)

as females and while no age group is excluded the condition tends to occur mainly in patients between the eighteenth and thirtieth years

Etiology —The etiology of regional ileitis is unknown The author subscribes to the view that it is a *psychosomatic disturbance* originating on the basis of a *hypersthenic intestinal neurosis* (p 1846) Organicists who do not share this view suggest that the disease is an attenuated form of *tuberculosis* (p 1860) or a variant of *acute ulcerative colitis*

Pathology —The gross findings in regional ileitis are quite remarkable The bowel thickened and stenosed The serosa is reddened and granular and the regional lymph nodes are hyperplastic The ileocecal valve thickened and the inflammation may extend to the cecal side The mucous membrane reveals shallow irregular *ulcers* along the mesenteric borders In more advanced examples the ulceration extend deeper and there is *polypoid hypertrophy* of the affected membrane The involved gut becomes *adherent* to adjacent intestinal loops bladder or abdominal wall *Penetration* with the formation of *fistulas* occurs and *abscesses may form around the site of ileal ulcers In approximately 15 per cent of* patients the fistulization of the ileal abscess reveals itself externally in the anal region There is commonly an increased amount of serosanguineous peritoneal fluid

Histologically the disturbance reveals hypertrophy of the muscularis and of the submucosa with fibroblastic reaction adjacent to the ulceration The inflammatory process may proceed to scarring with resultant intestinal obstruction but in favorable examples the bowel returns to approximately normal

Clinical Manifestations —The pathological description of regional ileitis suggests that the disease is capable of appearing in a variety of forms

DIFFERENTIAL DIAGNOSIS OF

Constipation

Constipation may be defined as a disturbance of intestinal function characterized by prolongation of the evacuation time for the individual Many patients evacuate every second, third or even fourth days while others are constipated if they do not have a bowel emptying after each meal Alteration in the individual rhythm of evacuation is the important variant.

The gastrocolic reflex sets up the sequence of events that leads to defecation. Ingestion of food starts a rush movement which usually traverses transverse and descending colons until the rectum and sigmoid are filled with the fecal mass The individual notes a desire to evacuate the sensation being referred to the suprapubic region, over the coccyx and adjacent regions or in the perineal and perianal areas If the reflex is heeded, evacuation is accomplished without delay through a complex phenomenon which involves contraction of abdominal musculature elevation of levator ani and relaxation of the anal sphincter the latter component alone being under voluntary control

If the defecation reflex is not heeded rectum and sigmoid develop an elevated threshold to the distention stimulus so that increasing amounts of stool accumulate before the desire to defecate is noted This abnormality constitutes the condition of dyschezia or rectal constipation in which the fecal mass dries inspissates and is evacuated only with difficulty and trauma (Fig 412)

In the majority of individuals constipation causes no symptoms Most often the colon conscious patient develops discomfort after reading or hearing about the absorption of harmful poisons a form of propaganda promulgated mostly by those who profit from the sale of cathartics This statement must not be interpreted to mean that the condition of auto-intoxication is not real and genuine A number of patients note fatigue drowsiness headache and malaise when they do not have a complete movement, and they are relieved of these symptoms when the lower bowel is emptied

Constipation may be the result of the operation of a variety of digestive and extradigestive causes A painstaking investigation is often required in order to elucidate the etiologic mechanism The complaints of recent constipation or of increasing obstipation merit complete radiography and extensive laboratory investigation since they suggest the presence of progressive organic disease possibly malignant.

	DIAGNOSTIC FEATURES
Errors in Hygiene	Starvation Insufficient food or water Low residue diet. Diminished tonicity of abdominal musculature Loss of anorectal reflex. Persistent vomiting Following catharsis
Ano Rectal	Dyschezia with loss of anorectal reflex and dilatation of rectal ampulla Fecal impaction Hemorrhoids fissures strictures, inflammations and malignancies of the lower bowel Supplement digital examination with anoscopy and sigmoidoscopy (p 1907)
Gastric	Acute dilatation of stomach with pyloric obstruction or retention All conditions associated with vomiting Gastrovisceroptosis Hypertrophic pyloric stenosis of infancy Aspirate stomach to determine gastric residue (p 3721) Get barium x ray (p 3742)
Colonic	With atony or spasmosis of bowel With coloptosis Hirschsprung's disease (congenital megacolon) strictures and organic intestinal obstruction, particularly of neoplastic origin Get x ray examinations with barium meal and enema (p 1824) Examine stools for occult [illegible] and perform sigmoidoscopy (p 1907)

CONTINUED

With *acute ulceration* there are manifestations indistinguishable from those of acute appendicitis (p 1881) with the finding of a large mass in the right lower quadrant *Subacute processes* are more insidious and produce a prolonged fever with diarrhea anorexia and progressive wasting The *syndrome* is *nonspecific* until a mass is felt in the right lower quadrant *or roentgenographic* examination demonstrates the presence of the lesion *in the* ileum Regional ileitis may first reveal itself by the appearance of *complications* such as intestinal obstruction (p 1873) or the development of a *fistula in ano* (p 1914) A number of patients have a laparotomy for acute appendicitis the correct diagnosis is suspected when convalescence is complicated by delayed wound healing or the development of a fecal fistula

The characteristic clinical finding in regional ileitis is the firm cigar shaped or irregularly spherical mass in the *right lower quadrant* (p 1886) The lesion is also palapable by rectum and may be associated with a drain ing sinus tract usually perineal

The barium enema reveals the presence of an extrinsic mass which in dents the cecum The regurgitation of the opaque mixture into the ter minal ileum may outline a spastic and irregular deformity *of this segment* of the small bowel These findings are confirmed by the barium meal

Diagnosis—The diagnosis of regional ileitis is most often made at opera tion or autopsy In the presence of a lesion in the right lower quadrant it is only natural that the first thought is the possible presence of an ap pendiceal abscess or a tumor of the cecum The simultaneous presence of a sinus tract or a fistula arouses the suspicion of the astute physician but absolute identification of the condition must wait upon exploratory lap arotomy since roentgenographic evidence is difficult of demonstration and interpretation Expert roentgenologists make serial ob ervations at hourly intervals for six hours after the barium meal Increased motility is a con stant finding More characteristic are fixed irregularities in outline nar rowing of the lumen changes in the mucosal pattern and demonstrations of internal fistulas

Treatment—The conservative treatment of regional ileitis is most un satisfactory The general principles are identical with those employed in the psychosomatic gastric disturbance of *peptic ulcer* (p 1780) Attempts at specific therapy by the injection of *antidysentery preparations* and the use of the *sulfonamide* drugs have been uniformly disappointing Strepto mycin (p 103) warrants extensive trial by combined oral and parenteral administration

Sooner or later the majority of seriously affected patients come to surgery Most often operative interference is undertaken under the mis taken assumption that there is pre ent an appendiceal abscess or a cecal neoplasm If the condition is recognized the surgeon should resect the ter minal ileum cecum and ascending colon and establish an anastomosis (p 1832) between ileum and transverse colon As an alternative a simple ex clusion operation is performed with transection of the terminal ileum proximal to the lesion and anastomosis of the upper loop of ileum to transverse colon

Despite the extent of the technical procedure the operative risk in regional ileitis is comparatively slight (5 per cent) as compared with the



Fig 413—*A* Case F B Graduate Hospital University of Pennsylvania December 1935 Roentgenogram of a barium enema showing the string sign one year previous to our examination of the patient

B Case F B 1936 Roentgenogram taken six and a half hours after barium meal showing extensive involvement of the terminal ileal loops

C Case F B May 1937 Specimen removed consisting of 2 feet of terminal ileum ileocecal valve and half of ascending colon

D Case F B Specimen shown in *C* opened showing the mucosal surface of the resected ileum and colon and the long constricted area with its thickened meso and hypertrophied fat completely encircling the serosa The mucosa of the cecum is normal (lower left) *

* Bockus Johnson and Lee in Frank H Lahey Birthday Volume C C Thomas Publisher

movements followed by a variable number of liquid motions The latter are preceded by cramps and eventually the stool is observed to contain blood mucus and pus As the condition progresses as many as forty to sixty movements occur daily The patient becomes progressively debilitated dehydrated and toxic

At times there may be a more acute onset due to the appearance of complications After weeks or even months of minor disturbances the patient develops an acute abdominal syndrome (p 1748) due to *penetration* or *perforation* of the ulcer or the formation of a *localized abscess* Later the tendency toward scarring produces the clinical syndrome of an intestinal obstruction (p 1873)

The routine physical examination affords very little assistance in the diagnosis of chronic nonspecific ulcerative colitis In the acute phase the



Fig 414—Adynamic ileus in peritonitis There is generalized distention of small and large intestines The loops are rather widely separated perhaps by exudate

patient appears severely ill dehydrated pale and weak The skin has an almost characteristic greenish hue The abdomen may be distended and there are evidences of peritoneal irritation such as spasticity and direct and rebound tenderness Rectal examination reveals a tight anal sphincter and a velvety feel to the rectal mucous membrane The finger upon being withdrawn is stained with a small amount of bloody purulent material This finding leads to *sigmoidoscopic investigation* as the result of which the characteristic findings elsewhere described (p 1856) are revealed

The *specimen* obtained by sigmoidoscopy and the stools reveals the presence of *mucus pus* and *red cells* with only an insignificant amount of feces Microscopic examination often shows *large mononuclear phagocyte*

hazards of the slow and unfavorable progression of the affliction The rate of recurrence following ileocolostomy is stated to be only 13.8 per cent

CHRONIC NONSPECIFIC ULCERATIVE COLITIS

Chronic nonspecific ulcerative colitis is a complicated clinical disorder which requires exact *definition and understanding* The name implies that it is an *inflammatory ulcerating disease* of the *large intestine* it is *chronic* and characterized by waves of *exacerbation* and *remission*, it is *nonspecific* since investigation has failed to reveal a definitive etiology such as the presence of the bacilli of dysentery or tuberculosis or the *Endamoeba histolytica*

Etiology—Chronic nonspecific ulcerative colitis has clearly recognizable predispositional factors The disease tends to occur in individuals of either sex during the second to fourth decades of *life* There are evidences of a preexistent *autonomic imbalance* and of *emotional instability* The initial attack or the recurrence of the disturbance is usually provoked by some *psychogenic factor* most often an emotional crisis Since the affliction usually involves single persons and the provocative circumstance is often in the nature of a frustration in a love affair or the death or illness of a parent or near relative the psychiatric implications cannot be avoided

The author is committed to the hypothesis that chronic nonspecific ulcerative colitis is a *psychosomatic disturbance* that is superimposed upon a *hypersthenic intestinal neurosis* As in regional ileitis (p 1853) this view is not shared by organicists some believe the disturbance results from long standing *bacillary* or *amebic colitis* or from primary infection by the normal intestinal inhabitants such as the *colon bacillus* or the *enterococcus* Bargen has isolated a specific *diplostreptococcus* which he believes causative and Schwartzman favors the view that the condition is precipitated by organisms and their toxins acting upon a segment of bowel that has been previously sensitized by the bacilli or amebae of dysentery staphylococci enterococci or coliform bacteria

Pathology—Nonspecific ulcerative colitis usually begins in the rectum or the *rectosigmoid* region though the entire colon is eventually involved Additionally in the more severe examples the *terminal ileum is also affected* *The earliest lesion is an edema and congestion* of the colonic mucosa This is followed by petechial hemorrhages and lymphoid hyperplasia with minute ulcerations Sigmoidoscopy reveals the lesions as finely granular areas with pin point yellowish to red flecks covered by patchy white exudate As the ulcers spread and coalesce large irregular circular or longitudinal lesions are observed The entire mucous membrane is friable and bleeds easily In the more severe instances abscesses involve the wall of the gut and the inflamed mucosa between the ulcers becomes hypertrophic and polypoid

With healing of the ulceration a large amount of scar tissue is laid down, resulting in the formation of a generalized tubular *stricture* which may progress to intestinal obstruction As in regional ileitis local abscesses perforation with resulting peritonitis and fistula formation occur as complicating conditions In favorable cases almost complete healing is observed

Clinical Manifestations and Diagnosis—The clinical manifestations of chronic nonspecific ulcerative colitis may be *insidious* or *acute* Most often the patient notes *malaise weakness indisposition generalized aches and pains and headache* with or without fever The earliest presenting symptom is a *diarrhea* which begins with the passage of one or more solid

monstrable but the organism that is isolated should not be misinterpreted as the etiological agent since it is rather a terminal invader

Systemically the patient becomes debilitated and develops a secondary *anemia* Metabolic disturbances are the rule rather than the exception since the diet is limited and absorption is seriously impaired Patients develop *avitaminoses* (p 616) and manifestations of *hypoproteinemia* (p 706) giving rise to the clinical picture of a *nephrosis* (p 2389)

With the onset of complications patients become physically and emotionally demoralized The skin loses its normal texture and bed sores and atrophic ulcers are encountered The necessity for constant movement of the bowels often results in a refusal of the patient to leave his bed pan Eventually even a courageous individual becomes progressively more discouraged and enters into a negativistic phase refusing to aid or cooperate in any manner In this late stage the patient may develop clubbing of the fingers (p 2878) and an arthropathy (p 2855) very similar to that seen in rheumatoid arthritis (p 2910) Since the latter disturbance also occurs in young patients who present identical emotional and vegetative patterns and since moreover the sufferer from rheumatoid arthritis tends to develop terminally a nonspecific ulcerative colitis there is a great temptation to interpret the two disturbances as different reaction pictures of a fundamentally similar affliction

Course —Chronic nonspecific ulcerative colitis runs a prolonged course punctuated by *remissions* and *exacerbations* In a small group of patients the disturbance is continuous Once the affliction has been established any number of factors tend to precipitate recurrences These include intercurrent infection emotional disturbances and overwork Eventually the milder manifestations abate and a complete cure may be experienced In the more unfortunate the condition continues for years with death resulting from toxemia or some complication

Treatment —The treatment of nonspecific ulcerative colitis is complicated and unsatisfactory The general principles laid down for the management of any *psychosomatic affliction* (p 1344) are followed no matter what curative form of attack is contemplated At different times almost every variety of medication and surgical procedure has been advised attempted and reported upon successfully The tendency of the disease to wax and wane makes it difficult to evaluate the efficacy of the allegedly specific modality

Nonspecific Therapy —Conservative treatment is based upon general *supportive therapy* A *low residue diet* (p 668) is given If the patient is dehydrated *fluids* are administered parenterally The judicious use of *small transfusions* is most salutary Because of the difficulties of absorption the *accessory minerals* and *available vitamins* particularly of the B complex are administered orally and parenterally The anus rectum and surrounding skin require the most expert and patient nursing attention If defecation is painful an anesthetic preparation such as 10 per cent ethyl amino benzoate or 1 per cent cocaine is applied before stool It is usually necessary to resort to opium for symptomatic relief The antispasmodics are of no avail but *Demerol* (p 3863) may prove useful

Cleansing *enemas* of saline are often comforting as are rectal instillations of warm olive cottonseed or cod liver oil Attempts at *local chemo*

cells which may be difficult to distinguish from amebae (p 524) Concentrated specimens are stained and examined for the presence of *tubercle bacilli* (p 52) Warm stage examinations are required for the demonstration of the *Endamoeba histolytica* (p 53) and cultures are made on special media for the growth of specific *dysentery bacilli* It is only when these examinations are negative that the diagnosis of the nonspecific type of ulcerative colitis can be considered

Radiography of the colon reveals first an extremely spastic and irritable bowel through which the enema runs with great rapidity The bowel appears shrunken shortened narrow and tubular, haustral markings are absent and the wall seems thickened and infiltrated, the mucosa is smooth In later stages irregular minute serrations are observed indicative of ul



Fig 415—Diffuse ulcerative colitis *

ceration The borders of the ulcers are uneven fringed and feathery In the reparative stage when scarring and fibrosis have occurred there is rapid filling of the bowel by barium enema and hyperirritability of the involved segments If polyps have developed their presence may be radiographically demonstrable

Complications—The complications of chronic nonspecific ulcerative colitis are distant or local immediate and remote

Locally the ulcers may *perforate* or *penetrate* giving rise to manifestations suggesting the presence of an *acute peritonitis* (p 1923) With the formation of strictures there occur mechanical difficulties due to subacute or chronic *intestinal obstruction* (p 1873) Bacterial invasions are easily invited through the ulcerating lesions In agonal states *bacteremias* are de-

* Buckstein Clinical Roentgenology of the Alimentary Tract



Fig 416—Intestinal tuberculosis Note particularly narrowed ileum with fistulous tracts also narrowed cecum with small translucent areas within it



Fig 417—Intestinal tuberculosis

therapy using medicated retention enemas are rarely helpful The recommended preparations include *azochloramid* in oil (1 2000) and *acriflavine* (1 4000)

Specific Therapy—The specific substances which have been tried include *vaccines* prepared with the Bargen diplostreptococcus the dysentery *bacillus* the typhoid paratyphoid organisms and autogenous coliform or streptococcal preparations *Antiserums* are available for dysentery coli and Bargen organisms These often produce severe reactions followed by an amelioration of symptoms as a nonspecific protein effect Anti B coli *bacteriophage* has been tried Antibiotic therapy with soluble and insoluble sulfonamide (p 88) and parenteral penicillin and streptomycin (p 106) merit extensive and thorough trial *Anti amebic therapy* with *emetine* (p 529) or *carbarsone* (p 530) is advisable as a therapeutic test Intensive courses of penicillin (p 106) are worthy of trial since they cause no injury

The multiplicity of the suggested treatment procedures is indicative of the relative inefficacy of each Probably none of the specifics is really curative Such fortunate results as are happily encountered indicate the healing force of nature The others are as tragic as any of the malignant conditions encountered in clinical medicine

Surgery—With a progressively unfavorable course surgical intervention should be considered Surgical intervention cannot well be avoided with impending perforation It is an important function of the practitioner to recommend operative intervention before the patient becomes too debilitated to withstand the necessarily formidable procedures When the disease is limited to the right half of the colon (10 per cent of patients) ileosigmoidoscopy with resection (p 1832) is desirable In this way the rectum is preserved With involvement of the left colon and rectum the procedures include ileostomy (p 1832) subtotal colectomy (p 1832) and proctectomy (p 1832) by multiple stages The mortality of ileostomy approximates 20 per cent and of colectomy 10 per cent

The care of the ileostomy must be fastidious to avoid social ostracism The patient eats a high caloric low residue constipating diet He takes little or no fluid after six P M He must have two or more well fitting colostomy bags with removable paper linings The skin around the stoma is protected with kaolin or a tenacious ointment such as aluminum paste or a mixture of cod liver oil and zinc oxide ointment

INTESTINAL MANIFESTATIONS OF SYSTEMIC INFECTIONS

Acute or chronic enterocolitis accompanies many of the systemic infections notably *typhoid fever* (p 275) the salmonella infections (*paratyphoid fevers*) *dysentery* (p 243) and *cholera* (p 249) Each of these disturbances is separately discussed elsewhere In the present place only the tuberculous infections are considered

TUBERCULOSIS OF THE INTESTINES

Tuberculosis of the intestine may be manifest as the primary infection or as end organ involvement secondary to a chronic focus in the lungs



Fig 416—Inte tin l t iberculo is Note part cularly narrowed ileum w th f tul us tra t also narrowe l cecum with small translucent areas w th in t



Fig 417—Inte tinal tuberculos

The Primary Intestinal Infection—In infancy, the small intestine may be the *portal of entry* with the production of the primary intestinal infection (p 255) Almost without exception this type of infection is produced by the ingestion of unpasteurized milk derived from tuberculous cows

In younger children the tuberculous infection gives rise to an *acute* or *chronic enteritis* as multiple tubercles involve the entire small bowel from the ligament of Treitz to the ileocecal valve In older children the symptoms are due to *caseation of the lymph nodes* particularly the group in the region of the meso appendix This latter syndrome known as *tabes mesenterica is usually mistaken for appendiceal inflammation* The child complains of attacks of *lower abdominal pain* sometimes localized in the right quadrant There may be evidence of peritoneal irritation with tenderness and rigidity Constitutional reactions are frequently present as manifested by fever and leukocytosis On rare occasions the diagnosis is made before operation when a radiograph reveals calcific shadows

Treatment is best conducted by the performance of a laparotomy with removal of the involved lymph nodes and appendix The postoperative course is eminently satisfactory

End Organ Intestinal Tuberculosis—Secondary intestinal tuberculosis is encountered much more frequently than the primary variety It usually occurs in the late stages of a pulmonary invasion and rarely is seen in those who are progressing favorably The obvious explanation for the intestinal lesion is the ingestion of virulent tubercle bacilli from open discharging cavities but it is more likely that the affliction is *hematogenous* since it usually involves the terminal ileum just proximal to the ileocecal valve and the first portion of the cecum

Hypertrophic granulomas and *ulcerating lesions* may occur in the tuberculous intestines The tuberculous ulcer of the small intestine is usually transverse and its healing leads to stenosis These lesions are associated with an enormous mass of mesenteric lymph nodes which eventually become caseous Numerous tubercles are usually present on the serosal surface as well Surprisingly few tubercle bacilli are demonstrable in these lesions

Clinical Manifestations—The superimposition of intestinal tuberculosis in the course of pulmonary infection is manifested by the appearance of *abdominal cramps* and *diarrhea* The stools contain blood and pus the patients become progressively more toxic and dehydrated while the fever and leukocytosis increase Sooner or later a firm tender *mass* is felt usually in the *right lower quadrant* The barium enema in association with the barium meal shows marked irritability and spasm in the terminal ileal segment and cecum It may not be possible to recognize where ileum leaves off and cecum begins *The definitive diagnosis of* tuberculous enterocolitis is established by the demonstration of tubercle bacilli in smears cultures or by guinea pig inoculation using a fecal suspension

Treatment—The treatment of intestinal tuberculosis is most discouraging Enthusiasts speak highly of the success of a rich vitamin diet combined with tomato juice and cod liver oil Heliotherapy (p 3704) is also highly regarded by its advocates and good results have been reported by roentgen therapy Opium is required as a palliative and calcium salts af

ford symptomatic relief The latter may be given orally as calcium lactate 2 0 gm (30 grains) or calcium gluconate 4 0 gm (60 grains) after meals Acute pain may be relieved by intramuscular injection of the gluconate or the intravenous use of 5 to 10 cc of 5 to 10 per cent calcium chloride

Surgical intervention is hazardous and holds little promise of relief Specific therapy with streptomycin (p 104) merits extensive and thorough exploration Pneumoperitoneum may be considered

CHAPTER 93

CLINICAL DISTURBANCES OF THE INTESTINES LOCAL LESIONS WITH OR WITHOUT SYSTEMIC MANIFESTATIONS

Besides manifestations of systemic disturbances (p 1839) the intestines may reveal local lesions of congenital traumatic mechanical inflammatory neoplastic or helminthic origin

CONGENITAL ABNORMALITIES

MECKEL S DIVERTICULUM

Meckel s diverticulum is formed by the remains of the *vitelline* or *omphalomesenteric duct* which joins the umbilical vesicle and the alimentary canal in early fetal life It usually consists of a pouch about 2 inches long which projects from the lower part of the ileum approximately 2 or 3 feet from the ileocecal valve The diverticulum may exist as a tubular structure or a solid fibrous cord It may be free in the peritoneal cavity or be attached to the anterior abdominal wall It is present in about 2 per cent of individuals

Clinical Manifestations —Persistence of Meckel s diverticulum rarely gives rise to symptoms As clinical curiosities the anomaly causes *pain* or *bleeding* when ulceration or erosion occurs in the ectopic gastric tissue contained in the walls of the pouch Under these conditions the symptom complex resembles that of *peptic ulcer* (p 1780) except that the pain is felt at or below the level of the umbilicus With erosion of a vessel there is a sudden appearance of *melena* (p 1843) or more rarely *hematemesis* (p 1764) when the blood is transported to the stomach by reverse peristalsis

Clinically the most that can be achieved in *diagnosis* is to suspect Meckel's diverticulum It cannot be definitively demonstrated except at exploratory laparotomy or autopsy

Treatment is surgical by excision

ECTOPIC GASTRIC MUCOSA

Ectopic gastric mucosa is found in portions of the small intestine A likely site is the upper segment of the jejunum just distal to the region of the ligament of Treitz The anomaly may produce the extremely rare *primary jejunal ulcers* which have a tendency to bleed and are recognized at operation or autopsy



Fig 418—Meckel's diverticulum

ECTOPIC PANCREATIC MUCOSA

Ectopic pancreatic glandular tissue may be found in any portion of the small intestine To the best of present knowledge these islands do not produce clinical symptoms

POLYPOSIS OF THE COLON

Congenital polyposis of the colon consists of multiple polypoid *adenomas* The condition is most frequently observed in children and young adults and apparently is somewhat more common in the *male* There is a strong *familial incidence*

The polyps vary from pea size to pedunculated tumors several centimeters in diameter Frequently the entire colon is involved but occasionally the lesion is localized to one or more segments As the result of the

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CHAPTER 93

CLINICAL DISTURBANCES OF THE INTESTINES LOCAL LESIONS WITH OR WITHOUT SYSTEMIC MANIFESTATIONS

- Congenital Abnormalities
  - Meckel s Diverticulum
  - Ectopic Gastric Mucosa
  - Ectopic Pancreatic Mucosa
  - Polyposis of Colon
  - Diverticulosis and Diverticulitis
  - Megacolon (Hirschsprung s Disease)
- Physical Chemical and Mechanical Injuries
  - Enterocolitis of Chemical Origin
  - Enterocolitis of Physical Origin
  - Penetration and Perforation
  - Intestinal Obstruction
  - Volvulus
  - Intussusception
- Infections and Inflammations
  - Acute Gastroentero-colitis
  - Nonspecific Granulomas of the Intestines
  - Appendicitis
  - Epiploitis
  - Mesenteric Lymphadenitis
- Neoplasms
  - Benign Tumors of the Intestines
  - Cancer of the Intestines
  - Carcinoid
- Infestations
  - Giardiasis
  - Balantidiasis
  - Helminthiasis
    - Distomiasis
    - Teniasis
    - Oxyuriasis
    - Uncinariasis
    - Strongyloidiasis
    - Ascariasis
    - Trichinuriasis

BESIDES manifestations of systemic disturbances (p 1839) the intestines may reveal local lesions of congenital traumatic mechanical inflammatory neoplastic or helminthic origin

CONGENITAL ABNORMALITIES

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Urinary	With pyelitis ureteritis and impaction of calculus Examine urine for erythrocytes and leukocytes (p 3683) Get ... out film for radiopaque shadows (p 3741) Summon urologist for cystoscopy and urograms (p 2248)
Hemic	In hemolytic crises with jaundice and anemia

action of the fecal current the pedicle of the polyp becomes attenuated and terminates in a large bulbous knob

The congenital polyps differ in morphology from those found in chronic infections of the colon (p 1860) such as tuberculosis chronic nonspecific ulcerative colitis amebic dysentery or chronic bacillary dysentery They have a tendency to undergo *malignant transformation* giving rise to *adeno carcinomas* (p 1888) which are not infrequently multiple Whether benign

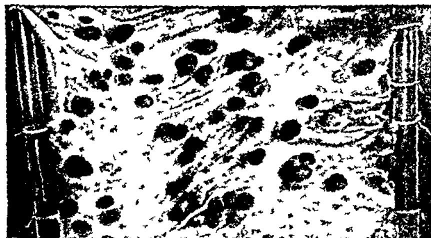


Fig 419 —Multiple polypoid adenomata of the mucosa of the colon

or malignant polyps have a tendency to *ulcerate* especially when they are present in the left half of the colon

Clinical Manifestations —Congenital polyposis is usually silent The condition may be revealed by routine examination of members of an afflicted family When disturbances are present the patient complains of recurring periods of *diarrhea* with the passage of frequent mucoid bowel movements which may or may not contain blood The diarrhea varies in intensity and may be mild or so intense as to be incapacitating Under the latter circumstances the patient presents manifestations of marked dehydration and loss of weight strength and appetite These may persist for days or weeks before disappearing only to recur in a more or less severe form Between bouts of diarrhea constipation may be present When the rectum is involved there are *tenesmus rectal urgency* and *melena* A severe secondary *anemia* (p 1055) may develop as a result of continuous slight oozing from innumerable small polyps

Carcinoma is the most frequent *complication* of multiple polyposis

MacCallum Textbook of Pathology

DIFFERENTIAL DIAGNOSIS OF

Pain in the Left Lower Quadrant

Pain in the left lower quadrant presents fewer diagnostic difficulties and problems than disturbances in the corresponding right quadrant In the male the possibilities narrow down considerably to involvement of the lower urinary tract and the sigmoid In the female there are the added considerations of lesions of the internal genitals

	DIAGNOSTIC FEATURES
Parietes	Lumbar myositis resulting from trauma or back strain
Intestinal	
Sigmoidal	With spasm diverticulitis and malignancy Perform igmoidoscopy (p 1907) and check findings with barium enema (p 1824)
Volvulus	With acute pain obstipation and passage of blood Prepare for laparotomy
Intussusception	Usually in childhood with acute pain and evidences of obstruction Attempt reduction with gentle enema and manipulation of mass (p 1877) Prepare for laparotomy
Intestinal Obstruction	With symptoms of dynamic ileus Prepare for laparotomy
Gynecologic	
Menstrual	With dysmenorrhea
Dysovulation	Recurrent pain midway in menstrual cycle Consider exploratory laparotomy
Ectopic pregnancy	With history of amenorrhea or irregular bleeding Note uterine enlargement and lateral mass Sedimentation time normal but urinary pregnancy test positive Summon specialist for laparotomy
Normal Pregnancy	From stretching of ligaments
Ovarian Cyst	With twist of pedicle Note mass in absence of evidences of infection.
Uterine Fibroid	Associated with degeneration Note irregular enlargement of womb Consider exploratory laparotomy
Salpingo-oophoritis	Of gonorrheal or tuberculous origin Note mass in fornix and rapid sedimentation time (p 3707) Get cervical smear for gonococci (p 50) If no response to anti infective therapy (p 106) consider laparotomy
Oophoritis	In mumps with parotid swellings
Pelvic Peritonitis	Following abortion or pregnancy May be associated with salpingo-oophoritis Employ intensive anti infective therapy (p 106)
Neurogenic	With neuritis or radiculitis secondary to zoster spinal cord tumor or neoplasm of cauda equina Look for motor and sensory changes for confirmation Obtain spinal fluid and consult neurosurgeon
Skeletal	Peferred pain from hypertrophic osteo-arthrosis of spine herniation of nucleus pulposus or low back strain Get x rays in various positions

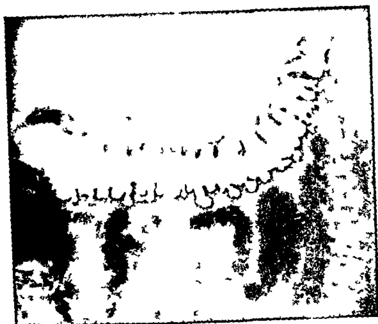


Fig 420—Diverticula of the colon

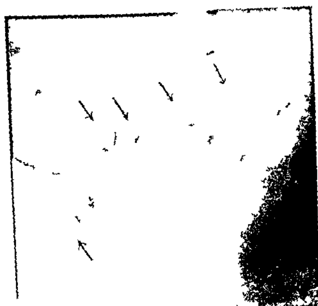


Fig 421—Diverticula of the colon same case as Fig 420 Showing detailed appearance of the sigmoid and of the diverticula

Buckstein Clinical Roentgenology of the Alimentary Tract

occurring eventually in 40 to 50 per cent of the afflicted The symptoms differ in no way from those occurring with the more usual types of malignancy of the colon (p 1888)

Aside from the pallor *physical examination* may reveal nothing of note Polyps present in the terminal colon are felt on digital examination *Sigmoidoscopy* usually reveals finely granular polyps which are not on a hyperemic inflammatory base and *are usually quite pliable and easily removed* A *biopsy* is made of several of the polyps especially those which are indurated or ulcerated suggesting malignancy *Radiographic* examination reveals a typical mottled appearance The *stool* practically always contains occult blood (p 3728)

Treatment —Since congenital polyposis presents a 50 per cent risk of malignant degeneration *surgical removal* of the affected bowel is a justifiable procedure It may be necessary to perform *total colectomy* (p 1836) and a permanent *ileostomy* (p 1832)

DIVERTICULOSIS AND DIVERTICULITIS

Diverticulosis is frequently observed in routine radiographic examinations of the colon The condition is usually *asymptomatic* and involves the descending and sigmoid portions of the bowel The sacculations probably initiate in an inherent weakness of the wall of the bowel With increased intracolonic pressure a pouch is formed At first the lesion is a small outpocketing of the mucous membrane but later it protrudes through the muscularis mucosae and finally through the external muscular layers to *reach the serosa*

As a rule the diverticula empty readily With retention however an inflammatory reaction or *diverticulitis* develops and this process leads to many complications and puzzling symptoms *A foreign body* may *lodge* within the lumen of the pouch and cause sufficient trauma to result in *perforation* the formation of a *localized abscess adhesion* of the gut to an adjacent viscus the formation of a *fistulous communication carcinomatous degeneration* or *stenosis* and *intestinal obstruction* from the contracting scar tissue of a healing lesion

Clinical Manifestations —Uncomplicated diverticulosis does not cause symptoms With a *simple inflammation* of the sac there may be localized pain and tenderness Associated spasm of the colon gives rise to cramplike abdominal distress usually localized in the left lower quadrant and the daily passage of several loose watery bowel movements containing varying *amounts of mucus and small amounts of blood* Between bouts of diarrhea the patient is often constipated

With *penetration* or *perforation* of the sac the pain becomes more severe and *is accompanied by fever chills and leukocytosis* Again the pain is localized to the left lower quadrant and the abdominal wall reveals varying degrees of involuntary rigidity With the formation of a *localized abscess* a mass is felt *Free perforation* into the general cavity produces the symptoms of *acute diffuse peritonitis* (p 1923) In contrast the *slowly progressive lesions* lead to the formation of granulomas which eventually produce occlusion of the sigmoid colon presenting a clinical picture that is indistinguishable from that of a *scirrhous carcinoma* (p 1888)

progressively a diverting proximal *colostomy* (p 1832) may be attempted After the lesion has healed the colostomy is closed

MEGACOLON (HIRSCHSPRUNG S DISEASE)

Hirschsprung s disease is a *dilatation* and *elongation* of the colon proximal to the rectosigmoid junction It is a rare condition and produces symptoms shortly after birth The condition may be due to an increased tone of the *adrenergic nerves* (p 1888) which produce a closure of the sphincters and a secondary dilatation of the colon Other alternative hypotheses suggest (1) A failure of relaxation of the internal sphincter of the rectosigmoid junction with proximal dilatation of the colon and (2) kinking of a congenitally elongated sigmoid with dilatation of the gut In any event



Fig 42 —Hirschsprung s disease Note essentially normal size of rectum *

the dilatation of the lumen is associated with muscular hypertrophy of the gut and a superficially inflamed and eroded mucous membrane

Clinical Manifestations —The outstanding clinical manifestations of Hirschsprung s disease are *abdominal distention* and *obstinate constipation* appearing shortly after birth Attacks of *abdominal pain* are frequent and the derangement of colonic function results in *anemia* *malnutrition* and *arrested growth* A quite characteristic observation is the passage of huge amounts of stool following an irrigation or the administration of a laxative

Complications are frequently encountered in Hirschsprung s disease and include *volvulus* (p 1875) *perforation* with diffuse peritonitis and an in

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Diagnosis —Diverticula are readily demonstrable by radiography With complications laparotomy reveals the nature of the primary lesion

Treatment —Diverticulosis does not warrant any special form of therapy other than for prophylaxis The patient is informed of the diagnosis is advised to adhere to a *low residue diet* and to *lubricate the bowel*—from above by the oral ingestion of mineral oil and from below by a nightly retention oil enema The use of *Tincture of Belladonna* or its substitutes (p 3875) is advised to relax the accompanying intestinal spasm Hot *rectal irrigations* with physiological saline solution are often most grateful and *sitz baths* (p 3791) are comforting when the pain is acute and persistent

DIFFERENTIAL DIAGNOSIS OF

Swellings and Tumors in the Left Lower Quadrant

Swellings and tumors are encountered less frequently in the left lower quadrant than in the right lower quadrant It is not at all infrequent for the practitioner to be able to roll a spastic sigmoid in the lean individual but any mass other than this requires a radiographic survey by barium enema and sigmoidoscopy followed by laparotomy if the condition is not completely and satisfactorily clarified

	DIAGNOSTIC FEATURES
Colonic	Impaction of feces relieved by enema Spasm diverticulitis inflammation or malignancy of sigmoid Perform sigmoidoscopy (p 1907) and check with barium enema (p 1824) Examine stools for occult blood (p 3728) and amebae Frei test for lymphopathia venereum (p 472)
Volvulus	Acute intestinal obstruction with passage of bloody discharge Prepare for laparotomy
Intussusception	Acute intestinal obstruction in infancy and childhood Attempt reduction with gentle barium enema (p 1876) Prepare for laparotomy
Gynecologic	As right lower quadrant
Urinary	Enlarged or ptosed kidney Get urogram and do cystoscopy (p 2248)
Peritoneal	Localized absce s Prepare for laparotomy

In the treatment of complications *surgical intervention* is often unsatisfactory and the mortality is prohibitively high When perforation leads to abscess formation it is advisable to wait until there is sharp localization Antibiotic therapy with sulfonamides (p 88) streptomycin (p 104) and penicillin (p 106) may cause the abscess to subside or evacuate into the lumen of the gut It is often a source of great satisfaction to observe the completeness with which extensive inflammatory processes melt under observation

Should the abscess persist incision and drainage are necessary Attempts to deal with fistulas often involve unexpectedly extensive surgical repair with disappointing results If the pericolonic inflammation continues

or impalement The *symptoms course* and *treatment* of intestinal perforation are elsewhere discussed in detail (p 234) Prompt surgical interference is mandatory as soon as shock can be controlled sulfanilamide powder may be applied locally at the site of the lesion and anti infective treatment is given parenterally with streptomycin (p 104) and penicillin (p 100)

INTESTINAL OBSTRUCTION

Intestinal obstruction occurs in the small or large bowel It may be acute subacute or chronic and complete or incomplete It may or may not be associated with strangulation of the gut These variations result in the production of innumerable clinical manifestations

Etiology.—The causes of intestinal obstruction include kinking angulation and constriction of the bowel by *external adhesions bands* or the neck of the hernial sac twists of the bowel in *volvulus* telescoping in *intussusception* stenosing lesions from *scar formation* or *malignancy* foreign body occlusions from impaction by a *hair ball* a *large gallstone* a *fecalith hydrophilic medicaments* or *psyllium seeds* (p 1826)

Clinical Manifestations.—The symptoms of intestinal obstruction vary with the site degree of completeness and the speed with which the occlusion is accomplished The symptoms are qualitatively similar but vary in their intensity The high obstruction is tolerated less well than the low blockage An acute and a complete closure produces more violent distress than a slow and incomplete lesion In all instances there are noted severe *abdominal cramps vomiting distention* rapidly increasing *dehydration oliguria* and failure to obtain feces or flatus by normal evacuations or repeated enemas As the result of the loss of gastric and intestinal secretion the blood chloride and sodium figures fall the nonprotein nitrogen elements rise and an alkalosis develops

The *vomitus* consists of gastric content at first Later there is bile stained fluid and eventually fecal emesis is observed The first enemas may contain feces which happen to be present in the bowel distal to the obstruction but later washings return clear Sooner or later the obstructive symptoms are associated with the picture of peripheral shock (p 928) which adds to the gravity of the situation and to the operative morbidity and mortality

Abdominal auscultation (p 3567) discloses active rumbling in contrast to the silence that accompanies *paralytic ileus* (p 1878) The powerful peristaltic efforts may be palpable and in later stages visible *Radiographic examination* reveals clearly the dilatation of the proximal loops with the characteristic staircase appearance Fluid levels are seen in a well established stoppage In small intestinal obstruction the dilated loops are located in the mid abdomen whereas colonic distentions occur laterally By contrast the gut distal to the block is collapsed and not demonstrable on the films See Figs 423 424

Treatment.—The aims of nonoperative treatment are the relief of the obstruction decompression of the proximal bowel and correction of the disturbed electrolyte pattern *Reduction* is tried when the stoppage is due to incarceration of a hernia (p 1800) or intussusception *Manipulation* is attempted with the hernia and the intussusception may be overcome by a barium enema given gently under fluoroscopic control The electrolyte

creased susceptibility to respiratory infections because of the encroachment upon the thoracic cavity of the abdominal distention

Physical examination reveals the tremendous abdominal distention and accompanying tympany Hard masses of stool are felt by abdominal or rectal palpation *Radiography* shows large amounts of gas in the colon and a tremendous dilatation of the lumen See Fig 422

Treatment—The conservative treatment of Hirschsprung s disease consists of the use of a *low residue diet* (p 668) supplemented by the daily use of *saline laxatives* (p 1830) To prevent the possibility of fecal impaction, *enemas* are given every second or third day Intramuscular injections of prostigmine (1 4000) may be given twice daily in 1 or 2 cc dosage The use of smooth muscle depressants (p 3892) merits therapeutic trial

Surgical attempts to palliate the condition of congenital megacolon include *lumbar sympathectomy* (p 1394) section of the *presacral nerve* and *resection of sigmoid and colon with ileosigmoidostomy* None of these procedures has been consistently successful

PHYSICAL CHEMICAL AND MECHANICAL INJURIES

ENTEROCOLITIS OF CHEMICAL ORIGIN

The deliberate or accidental ingestion of irritating foods drugs poisons and bacterial toxins produces irritation of the intestinal tract which leads to *abdominal cramps* and *diarrhea* More specifically the causes for these common attacks of colly wobbles include the ingestion of concentrated fruit juices or unripe fruits such as green apples overdistention due to gluttony and the introduction of bacterial enterotoxins particularly those produced by the staphylococcus (p 240) The noxious ingestant may be a poison or an irritant drug such as a drastic or a concentrated saline laxative

Treatment consists in the application of heat to the abdomen and the use of opiates when pain is severe The administration of antispasmodics protectives and demulcents accomplishes very little Attempts to hasten the elimination of the offending material by purging add insult to injury Elimination may be hastened by the use of a cleansing enema

ENTEROCOLITIS OF PHYSICAL ORIGIN

Deep *roentgen therapy* (p 3796) and *hyperthermia* (p 3789) produce injuries to the intestinal tract Overdosage with these intended therapeutic agencies may give rise to nausea vomiting or diarrhea

PENETRATION AND PERFORATION OF THE INTESTINES

Intestinal penetrations and perforations occur in diseased and normal bowels In *intestinal penetrations* the peritoneal cavity is invaded through rupture of a peptic or typhoidal ulcer an inflamed appendix a diverticulum or a neoplasm Dehiscence of a suture line is a tragic event that complicates surgical procedures particularly those in which an anastomosis has been performed Obstructed and strangulated bowel becomes gangrenous and the weakened walls give way

In intestinal perforations the normal bowel may be perforated by a bullet wound or a crushing injury to the abdomen The gut may be torn in the course of a sigmoidoscopic examination or as the result of a stab wound

pattern is reestablished by a continuous intravenous drip using buffer solution as an infusate Plasma and whole blood are substituted in the presence of shock

Suction decompression of the small intestine by means of the Miller Abbott tube and the Wangensteen apparatus has revolutionized the conservative treatment of intestinal obstruction If the tube can be passed down to the site of the occlusion the collapse of the distended gut and relief of the edema of the wall may be sufficient to restore the integrity of the lumen of the bowel and obviate the necessity for operation

When conservative treatment fails *surgical intervention* is mandatory After the surgeon has relieved the occlusion he may be required to perform a *resection* and *anastomosis* (p 1836) if the gut is no longer viable or the obstruction is of a permanent or recurrent nature If the condition of the patient is at all grave it is the greater part of wisdom to perform a *palliative enterostomy* or *colostomy* (p 1836) leaving the more formidable procedure for a second session when general conditions have been bettered Meantime the intravenous fluids are continued and *anti infective therapy* is effected by parenteral use of streptomycin (p 104) and penicillin (p 106) and topical application at the operative site of sulfanilamide powder (p 88)

INTESTINAL OBSTRUCTION DUE TO FOREIGN BODIES AND FECAL IMPACTION

Obturation of the bowel occurs with obstructions within the lumen of the gut The blockage may be due to the presence of a *large gallstone* *inspissated feces* *intestinal helminths* the *hairball* the swelling of a *hydrophilic laxative* or a mass of *psyllium seeds* With the exception of the *fecal impaction* these conditions are relatively rare

Obstruction due to the presence of large amounts of *dried stool in the rectal ampulla* are frequent and often unrecognized This situation should be suspected when debilitated patients complain persistently of abdominal discomfort and distention unrelieved by cathartics and enemas The *diagnosis* often is obscured by frequent small movements which consist of fragments of inspissated material Under these circumstances the nurse or the medical record reports that an evacuation has occurred and the physician is diverted from arriving at the correct diagnosis unless he makes a digital examination of the rectum There the examining finger encounters dried stool which may have the feeling of concrete

The *treatment* of fecal impaction is most difficult for both patient and attendant The mass is broken up digitally Softening is aided by a retention enema of oil or hydrogen peroxide Thereafter the condition is prevented by the use of mineral oil by mouth oil retention instillations at bedtime and daily soapsuds enemas for cleansing during the course of the day

VOLVULUS

The volvulus or torsion of the bowel usually occurs in the *sigmoid flexure* less frequently in the *cecum* and *terminal ileum* The condition occurs three or four times more frequently in men than in women and is seen in its greatest incidence in middle and advanced years Reports from Russia and Serbia indicate that the condition is more often encountered



Fig 493—Spiral spring formation of small intestine (prone position) in acute intestinal obstruction *

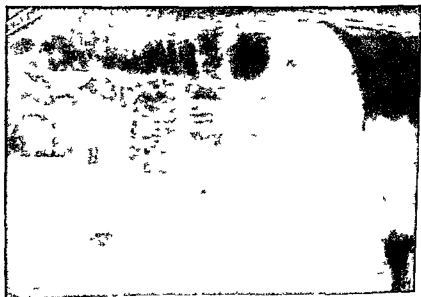


Fig 494—Showing gas-capped fluid levels in lateral position *

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months of life and is three times as frequent in the male as in the female More than three-quarters of all of the instances of intussusception are seen in children under the age of two The commonest site for the intus u cep tion is the *ileocecal junction* where vigorous ileal peristal is is countered by antiperistalsis in the cecum The condition may al o occur el ewhere in the small and large intestine

Intussusceptum and Intussuscipiens—The usual intussusception consists of three cylinders The internal and returning layers form the *intussusceptum* and the outer layer is the *intussuscipiens* The wall of the intu susceptum become edematous and engorged with blood Extravasation occurs into the lumen giving rise to the characteristic *bloody passage* Obstruction is never quite complete unless vascular occlusion leads to gangrenous change in the involved segment of the bowel See Fig 496

Clinical Manifestations—The clinical manifestations of intussu ception consist of periodic attacks of *pain* and *vomiting* with the passage of *mucus* and *blood* by rectum Examination reveals a *palpable tumor* in the *right lower quadrant* when the lesion involves the ileocecal segment In infant



Fig 496—Roentgenograms with contrast enema showing features of a t p al ileocol c in tussusception

who are unable to report symptoms the onset is heralded by a sudden spell of crying Digital examination by rectum reveals blood or the mother reports the sanguineous discharge on the diaper or stool

The *abdominal tumor* is usually felt as a banana shaped mass to the right of the umbilicus A characteristic of the tumor of intussusception is the *alternate stiffening and relaxation* that occurs with the peristaltic rush In contradistinction to volvulus (p 1875) there is *little distention* since obstruction is not *complete*

Treatment—On rare occasions the intussusception may be reduced by means of a *barium enema* administered under fluoroscopic control Surgical therapy consists of *manual reduction* of the defect through a short right rectus incision If the involved segments are not viable a *lateral anastomosis* (p 1836) must be performed and this procedure has a high operative mortality

Operative interference is indicated for *recurrent and chronic intussusception* The latter in the adult is often associated with Meckel s diverticulum (p 1864) which serves as an entering wedge

Ladd and Gross Abdominal Surgery of Infancy and Childhood

there than in the United States It is suggested that this finding is explained by the greater length of the intestine and the increased bulk of the Russian diet

The torsion may vary from 180 to 720 degrees The twist is more frequently clockwise but may be counterclockwise Invariably there are secondary circulatory changes in the afflicted loop with vascular occlusion distention gangrene and perforation of the twisted segment

Clinical Manifestations—The clinical manifestations of the volvulus are those of an *intestinal obstruction* (p 1873) When circulatory changes appear in the bowel there are evidences of *shock* and *peritoneal irritation* The diagnosis may be suspected before operation by the combined features of left lower quadrant pain evidences of intestinal obstruction and



Fig 495—Volvulus of the sigmoid Film taken in the recumbent position The tremendous dilatation of this loop of bowel is clearly demonstrated

the appearance of a palpable mass *Radiography* reveals collapse of the terminal bowel with gaseous distention proximal to the descending colon

Treatment—Mild torsion may occasionally be relieved by the gentle administration of a *barium enema* under fluoroscopic control Otherwise immediate *surgery* is mandatory In the early stages it is necessary merely to untwist the strangulated segment If there is doubt concerning the viability of the bowel the segment must be excised (p *1836*) and the technical difficulties of the procedure involve a formidable task

INTUSSUSCEPTION

The clinical condition of intussusception involves an *invagination* of the gut This accident occurs most commonly between *the fourth and ninth*

dietary indiscretion introduction of *staphylococcic enterotoxin* (p 240) infections with *salmonella* or the ingestion or excretion of *irritants* such as the *drastic cathartics* and the *heavy metals* It is possible also that enterocolitis may arise from the normal fecal organisms such as *Streptococcus faecalis* colon bacilli and the anaerobes akin to the Welch bacillus These conditions are most often grouped by the laity under the heading of ptomaine poisoning an obvious misnomer since preformed ptomaines are rarely encountered This error hinders a clear understanding of the etiology and management of these common disturbances

Clinical Manifestations —Acute gastro enterocolitis is manifested by abdominal distress *nausea vomiting* and *diarrhea* Attacks vary greatly in violence Those due to *staphylococcic enterotoxin* have particularly marked vomiting and a negligible period of latency The *Salmonella infections* are characterized by the profuse diarrhea and may not occur for several hours after the acquisition of the infection

A common type of gastro enterocolitis of nonspecific origin results from *dietary indiscretion* Children eat unbelievable combinations of food at parties and picnics adults offend the intestinal mucous membrane by the quantity and quality of refreshments at drinking bouts Sensitized individuals with food idiosyncrasy suffer from an intestinal upset akin to *contact dermatitis* (p 3330) when they ingest the specific digestive allergen Chance ingestion of cadmium and fluoride also may be provocative

Acute enterocolitis occurs in patients who are debilitated and suffering from chronic disease It is a *terminal manifestation* in *diabetic coma* (p 1257) and *uremia* (p 2276) Under these circumstances the complication is probably of the nature of a decubitus and is often *agonal*

Treatment —Acute gastro enterocolitis is usually self limited The therapeutic problem involves *discontinuance of the irritant* and the *prevention* or *treatment of dehydration* and the disturbances of the *electrolyte pattern* (p 5) We are opposed to drastic purging with castor oil saline or calomel since it tends to increase discomfort and augment the secondary metabolic complications It is our opinion that sufficient excretion is accomplished by the vomiting and diarrhea and that the further administration of irritants adds to the inflammatory process and the patient s discomfort

It is our practice to allay the symptoms by administering *opium* (p 3853) as soon as it is obvious that there has been sufficient emesis and diarrhea to fulfil the purposes of evacuation One teaspoonful of paregoric is given each time the patient evacuates *Heat* is applied to the abdomen and the patient is urged to take *fluids* and a *soft diet* as soon as the stomach is tolerant If the symptoms fail to abate it is necessary at times to set up an *intravenous drip* using glucose in physiological saline solution or a buffer infusate (p 3775)

The *antispasmodics* are of no value protection is best afforded by the ingestion of warm milk a thick cereal mashed potatoes or spaghetti It is wise to consult the patient s taste and permit the ingestion of the chosen foodstuff some prefer cold carbonated drinks and others desire salty foods or solids such as beefsteak which requires chewing The postdiarrheal constipation is best relieved by an enema

LOCAL INFLAMMATIONS AND INFECTIONS OF THE SMALL INTESTINE AND COLON

Local nonspecific inflammations and infections may involve the entire gut (*gastro enterocolitis*) or one of its component parts (*appendicitis epiploitis* and *mesenteric lymphadenitis*) The specific bowel infections such as typhoid and the dysenteries are discussed in the section on the infectious diseases *Marginal* and *jejunal ulcers* and *diverticulitis* are described respectively with the problems of peptic ulcer (p 1780) and diverticulosis (p 1868) *Regional ileitis* and *chronic nonspecific ulcerative colitis* are in

DIFFERENTIAL DIAGNOSIS OF

Tympanites (Flatulence, Meteorism)

Tympanites is recognized by the uniform distention of the abdomen due to the presence of gas within the lumen of the bowels Under these circumstances the percussion note is characteristically hollow and drum like dullness cannot be elicited in the flanks and the fluid wave that is characteristic of ascites (p 1921) cannot be demonstrated.

	DIAGNOSTIC FEATURES
Excessive Gas Production	Due to air swallowing copious ingestion of carbonated fluids fermentation of sugars in milk and fruit beverages, and gas production by putrefactive bacteria.
Adynamic Ileus (Silent)	
Postoperative	Often associated with acute dilatation of the stomach. Relieved by neostigmine or pitressin
Generalized Infection	With pneumonia and typhoid fever Relief from neostigmine or pitressin.
With Localized Infection	Particularly peritonitis following operation or in association with generalized infection.
Psychogenic	In hysteria Often associated with air swallowing
Neurogenic	Particularly with cord lesions such as transverse myelitis Following sympathectomy for hypertension.
Pharmacodynamic	Particularly following heavy dosages of opiates and general anesthesia
Dynamic Ileus	
(With Cramps and Borborygmi)	Intestinal obstruction. Get x ray for observations of obstructed and collapsed loops (p 3253)

cluded with the neurogenic and psychosomatic manifestations involving the gut (p *1344*) *Strangulation and incarceration* of the bowel are dealt with in the section on the hernias (p 1800)

ACUTE GASTRO ENTEROCOLITIS GASTRO ENTERITIS ENTERITIS AND COLITIS

Acute inflammations of the stomach the small intestine and the colon are encountered with *great frequency* Most often they are due to

dietary indiscretion introduction of *staphylococcic enterotoxin* (p 240) infections with *salmonella* or the ingestion or excretion of irritants such as the *drastic cathartics* and the *heavy metals* It is possible also that enterocolitis may arise from the normal fecal organisms such as *Streptococcus faecalis* colon bacilli and the anaerobes akin to the Welch bacillus These conditions are most often grouped by the laity under the heading of ptomaine poisoning an obvious misnomer since preformed ptomaines are rarely encountered This error hinders a clear understanding of the etiology and management of these common disturbances

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A common type of gastro-enterocolitis of nonspecific origin results from *dietary indiscretion* Children eat unbelievable combinations of food at parties and picnics adults offend the intestinal mucous membrane by the quantity and quality of refreshments at drinking bouts Sensitized individuals with food idiosyncrasy suffer from an intestinal upset akin to *contact dermatitis* (p 3330) when they ingest the specific digestive allergen Chance ingestion of cadmium and fluoride also may be provocative

Acute enterocolitis occurs in patients who are debilitated and suffering from chronic disease It is a *terminal manifestation* in *diabetic coma* (p 12o7) and *uremia* (p 2276) Under these circumstances the complication is probably of the nature of a decubitus and is often *agonal*

Treatment—Acute gastro enterocolitis is usually self limited The therapeutic problem involves *discontinuance of the irritant* and the *prevention* or *treatment of dehydration* and the disturbances of the *electrolyte pattern* (p 5) We are opposed to drastic purging with castor oil saline or calomel since it tends to increase discomfort and augment the secondary metabolic complications It is our opinion that sufficient excretion is accomplished by the vomiting and diarrhea and that the further administration of irritants adds to the inflammatory process and the patient s discomfort

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DIFFERENTIAL DIAGNOSIS OF

Pain in the Right Lower Quadrant

With pain in the right lower quadrant the physician s first thought is directed to the po si bility of an acute inflammatory process of the appendix It is h s prime obligation to eliminate the d agnosis of acute appendicitis before commission to some other etiologic mechanism

SITE	DIAGNOSTIC FEATURES
Parietes	Lumbar myo itis associated with trauma or low back strain
Intestinal	
Appendicitis	With acute inflammation or abscess Localized pain and tenderness confirmed by rectal ex amination (p 1181) With or without fever and leukocytosis Cons der exploratory laparotomy
Ileal	*Particularly with regional ileitis* simulating acute append citis May be later associated *with abdominal or perineal fistulas* D agnosis suggested by barium meal (p 1851) Con ider laparotomy
Cecal	With trapped *gas or feces and* pasmo[illegible] Penetration or perforation of malignancy or tuberculous infection *Observe* defect in barium enema Consider exploratory laparot omy
Tabes Mesenterica	Inflammation of *mesenteric lymph nodes fre* quently tuberculous or following upper respi ratory Laparotomy indicated
Urinary	With pyelitis ureteritis and impaction of cal culus Examine *urine for crystals* erythrocytes *and leukocytes (p 3667)* Get scout film for radiopaque shadows (p 2248) Summon urolo gist for cystoscopy and urograms
Gynecologic	
Menstrual	With dysmenorrhea but possibility of coexi t ent appendicitis should be kept in mind
Dysovulation	Recurrent pain midway in *menstrual cycle* Consider exploratory laparotomy (p 2028)
Ectopic Pregnancy	*With history of amenorrhea or irregular* bleed ing Note uterine enlargement and lateral mass Sedimentation time normal but urina y p egnancy *test positive (p 2496)* Summon specialist for laparotomy
Normal Pregnancy	From *stretching of* ligaments
Ovarian Cysts	With twi t of pedicle Note mass in absence of evidences of infection
Uterine fibroid	*A sociated with degeneration* Note irregular enlargement of womb Consider exploratory laparotomy
Salpingo-oophoritis	*Of gonorrheal post-abortal or tuberculous* origin Note mass *in fornix and rapid sedi mentation time* Get cervical smear for g no- cocci (p 50) *If no response to anti infective* therapy (p 106) consider laparotomy
Oophoritis	In mumps with swollen parotids

NUED

Pelvic Peritonitis	Following abortion or pregnancy May be associated with salpingo-oophoritis Employ intensive anti infective therapy (p 1?6)
Neurogenic	With neuritis or radiculitis secondary to zoster spinal cord tumor or neoplasm of cauda equina Look for motor and sensory changes for confirmation. Obtain spinal fluid and consult neurosurgeon
Hemic	In hemolytic crises with jaundice and anemia In capillary toxicosis (Henoch) with cutaneous purpura
Skeletal	Referred pain from hypertrophic osteoarthritis of spine herniation of nucleus pulposus or low back strain.

NONSPECIFIC GRANULOMAS OF THE INTESTINES

Inflammatory reactions involving segments of the intestinal tract may produce nonspecific granulomas These occur at the sealing off of a *penetration* as a reaction to a temporary *intestinal obstruction* in an *incarcerated hernia* after *diverticulitis* or during the course of a chronic nonspecific *ulcerative colitis* or a *regional ileitis*

The nonspecific granuloma produces the clinical symptoms of *intestinal obstruction or ulceration The condition may simulate the disturb*ances produced by a *malignant neoplasm* until the surgeon at operation happily encounters the benign process

APPENDICITIS

Inflammation of the appendix is the *most frequently encountered intra* abdominal condition Its frequency and the variability of its manifestations require that the practitioner consider its presence in dealing with any disturbance below the diaphragm and above the perineum

Etiology—*In the majority of instances* appendicitis is produced by *local causes* such as obstruction occlusion or stenosis of the lumen In rarer instances as for example *following the upper respiratory infection* acute appendicitis may be *hematogenous* in origin

Pathology—Consideration of the anatomy of the appendix reveals adequate explanation for the frequency with which it is diseased The organ is a *blind pouch* with terminal ascculature Its musculature is feeble and may be replaced completely by scar tissue Its dependent position at the base of the cecum, invites the inspissation of fecal material and there is little or no provision by which this vestigial organ may evacuate its contents Since appendicitis occurs more frequently in sedentary individuals it is likely that those whose occupations *involve physical labor or exercise* accomplish evacuation of the appendiceal lumen by frequent contractions of the abdominal musculature It is also suggested that the squatting position of those who evacuate in the great open spaces assists in the emptying of the appendiceal cavity and explains the lesser incidence of infection

The appendix may occupy any one of a variety of sites in the abdominal cavity Most frequently it is situated in the *right lower quadrant* but it may vary from a *pelvic* to a *subhepatic position* It may be wholly or partially *peritonealized* and it may occupy a position behind the peritoneal covering The *pathological processes that involve the appendix* are as varied as its localities The *mucosa* alone may be involved or the inflammatory process may extend through the wall and *serosa* The nature of the inflammation may be a simple catarrhal process but with vascular occlusion the organ becomes gangrenous The local peritoneal reaction may be *fibrinous* or *purulent* and there may be a diffuse peritonitis The venous radicles may be uninvolved or they become the sites of a *suppurative thrombophlebi*

DIFFERENTIAL DIAGNOSIS OF

Pain in the Right Lower Quadrant

With pain in the right lower quadrant the physician's first thought is directed to the possibility of an acute inflammatory process of the appendix It is his prime obligation to eliminate the diagnosis of acute appendicitis before commission to some other etiologic mechanism

SITE	DIAGNOSTIC FEATURES
Parietes	Lumbar myositis associated with trauma or low back strain
Intestinal	
Appendicitis	With acute inflammation or abscess Localized pain and tenderness confirmed by rectal examination (p 1181) With or without fever and leukocytosis Consider exploratory laparotomy
Ileal	Particularly with regional ileitis simulating acute appendicitis May be later associated with abdominal or perineal fistulas Diagnosis suggested by barium meal (p 1851) Consider laparotomy
Cecal	With trapped gas or feces and spasmodis Penetration or perforation of malignancy or tuberculous infection Observe defect in barium enema Consider exploratory laparotomy
Tabes Mesenterica	Inflammation of mesenteric lymph nodes frequently tuberculous or following upper respiratory Laparotomy indicated
Urinary	With pyelitis ureteritis and impact or of calculus Examine urine for crystals erythrocytes and leukocytes (p 3007) Get scout film for radiopaque shadows (p 2248) Summon urologist for cystoscopy and urograms
Gynecologic	
Menstrual	With dysmenorrhea but possibility of coexistent appendicitis should be kept in mind
Dysovulation	Recurrent pain midway in menstrual cycle Consider exploratory laparotomy (p 2528)
Ectopic Pregnancy	With history of amenorrhea or irregular bleeding Note uterine enlargement and lateral mass Sedimentation time normal but urinary pregnancy test positive (p 2496) Summon specialist for laparotomy
Normal Pregnancy	From stretching of ligaments
Ovarian Cysts	With twist of pedicle Note mass in absence of evidences of infection
Uterine fibroid	Associated with degeneration. Note irregular enlargement of womb Consider exploratory laparotomy
Salpingo-oophoritis	Of gonorrheal post abortal or tuberculous origin Note mass in fornix and rapid sedimentation time Get cervical smear for gonococci (p 50) If no response to anti infective therapy (p 106) consider laparotomy
Oophoritis	In mumps with swollen parotids

CONTINUED

cavity becomes involved in a *diffuse peritonitis* (p 1923) The patient is gravely ill and *sepsis* is an invariable accompaniment Surgical intervention under these circumstances is fraught with danger since the risk is great and the accomplishment limited by the mechanical impossibility of draining the entire intra abdominal region

The occurrence of gangrene and diffuse peritonitis is often accompanied by deceptive physical signs There may be a sudden cessation of pain suggesting an alleviation of the condition As an additional evidence of presumptive improvement rigidity diminishes and gives way to the clinical picture of a *soft belly peritonitis* The astute practitioner is not deceived by this mirage for he notes that the apparent relief of local manifestations is accompanied by increase in the systemic features The pulse rate becomes more rapid the patient appears to be more toxic the temperature may be a little higher and the leukocyte count considerably increased The onset of chilliness or actual chills strengthens the view that the situation is more ominous and suggests the possibility that there is an associated suppurative thrombophlebitis

It is at this time and under these circumstances that some surgeons elect to postpone laparotomy hoping to await the localization of the process Operative interference at this stage is accompanied by high morbidity and mortality Particularly since the introduction of the antibiotics deferred intervention seems the greater part of wisdom

Acute appendicitis may be accompanied before or after surgical intervention by pylephlebitis or the development of localized peritoneal abscesses particularly in the subdiaphragmatic areas (p 1927) Venous involvement is suggested by increasing toxemia and the presence of a swinging temperature with chills The localized abscesses reveal themselves by localized pain and tenderness

Recurrent Appendicitis—Recurrent appendicitis is a clearly defined clinical entity It consists of repeated attacks of right side itis and is due to repeated or multiple inflammations of the appendix The inflammatory process is of low grade intensity and patients may not even consult the practitioner until several attacks have been experienced Appendectomy is strongly advised lest a graver attack occur under less favorable circumstances

Chronic Appendicitis—The syndrome of chronic appendicitis as described by its adherents consists of varied intra abdominal complaints without any manifestation pointing directly to the vermiform appendix itself Thus when a patient complains of any of the manifestations of the gastric neurosis (p 1767) intestinal neurosis (p 1845) auto intoxication (p 1821) or constipation (p 1852) as well as the more tangible conditions of peptic ulcer (p 1780) or otherwise inexplicable hematemesis (p 1764) a chronic inflammatory process involving the appendix is suspected Operative removal is suggested and these patients note an immediate alleviation of symptoms

We who do not believe in the existence of chronic appendicitis point out that bed rest alone without laparotomy produces a similar temporary amelioration of complaints The late symptomatic results following appendectomy for chronic appendicitis are far from being as convincing as the more premature evaluations

tis giving rise to *abscesses in the liver* or the *subphrenic regions* With sepsis and bacteremia distant manifestations become apparent

The physician who recognizes the variability of the etiology anatomical location path ological involvement and associated complications realizes that there is no such thing as "typical appendicitis He approaches the differential diagnosis of any type of bellyache with the suspicion that the complaint is just one more disguise that is assumed by the prin cipal intra abdominal enemy

Clinical Manifestations—In its most usual form acute appendicitis is heralded by the sudden occurrence of *epigastric* or *peri umbilical pain nausea* and *vomiting* Diarrhea does not occur unless the patient is in judiciously and inadvertently given a purge

The initial referred pain of the visceral involvement persists for one to several hours and may or may not be accompanied by *fever* and *leuko cytosis* After a variable period the pain shifts to the *right lower quadrant* indicating a beginning peritoneal involvement It is at this time that most patients summon their practitioner Too often the affliction is regarded as an ordinary bellyache and is treated by purges provocative of com plications

With the localization of pain in the right lower quadrant the phys ician elicits sharply *localized tenderness* and *involuntary rigidity* (p 1476) The definition of *tenderness* is by far the most reliable early physical sign since rigidity may be absent until peritoneal irritation has occurred Ab dominal tenderness is corroborated by similar findings obtained by rectal examination

It is our unqualified opinion that *operation is imperative* in the pres ence of these herald symptoms We do not believe that it is justifiable for the practitioner to await the development of the full blown syndrome of muscular rigidity fever and leukocytosis since the presence of these indi cates that there is already more than purely local inflammation

In the hematogenous variety of appendicitis the patient develops ab dominal symptoms within twelve to thirty six hours following an upper respiratory infection most often a tonsillitis This sequence of events is more frequent in young children and robust young adults With it there may be a more considerable elevation of temperature than in appendicitis of mucosal origin

Course—In private practice the majority of patients with acute ap pendicitis are subjected to operation when the disturbance is limited to the local inflammatory changes Without surgical intervention the appendiceal inflammation may spontaneously abate but more likely will pass to the phase of complications

A certain amount of peritoneal reaction accompanies the mildest ex amples of appendicitis In the most favorable instances there is a laying down of *fibrin* With infections of greater severity a *localized peritonitis* develops and this may proceed to the point of suppuration as manifested by the appearance of a palpable mass discerned by abdominal or rectal examination In general the *appendiceal abscess* proceeds in one of three directions (1) It may resolve and *heal spontaneously* (2) it may rupture into the lumen of the bowel and *evacuate itself* in this satisfactory man ner (3) but most often if it is not drained surgically it leads to the development of a *diffuse peritonitis* or a *general sepsis*

With gangrene and perforation of the appendix the entire peritoneal

Pleuritis and *pneumonia* (p 2171) involving the right lower lobe are occasionally ushered in by pain in the right lower quadrant In the absence of *respiratory symptoms and signs* a laparotomy may be erroneously performed adding the anesthetic risk to the pneumococcal infection

Treatment—The treatment of appendicitis is *surgical* The practitioner is warranted in urging laparotomy when there is suspicion of appendiceal infection He should not temporize and enter into overelaborate differential diagnostication It is his function to summon the surgeon and proceed with*out delay unless the latter is willing to assume* responsibility for further observation The practice of *freezing* the involved appendix by the application of an ice bag is inexcusable Appendiceal surgery is preceded by and followed with parenteral injections of streptomycin (p 104) and penicillin (p 106) Topical application to the operative site of sulfanilamide powder may be considered An intravenous drip of saline dextrose and/or plasma is continued until fluids are taken freely by mouth

Appendectomy—Appendectomy is the commonest intra abdominal operation The procedure depends upon the pathologic nature of the appendix and the variety and intensity of the peritoneal reaction

Interval Operations—Interval appendectomy is performed as a procedure of choice at a time which is convenient the risk is negligible

Acute Appendicitis without Peritonitis—In acute appendicitis without peritonitis operation is attended with relatively slight risk except in the occasional instance in which a severe grade of appendiceal inflammation is complicated by *thrombophlebitis of the mesenteric veins* Under such circumstances the thrombophlebitis may extend into the portal radicle establishing a pylephlebitis (p 1961)

With the *appendix unruptured* the operative procedure consists of excision of the appendix and cauterization of the stump drainage is unnecessary

Acute Appendicitis with Localized Peritonitis—With appendicitis and local peritonitis or abscess formation the peritoneal infection may result from direct extension through the wall of the viscus or from actual perforation In addition to removal of the appendix drainage of the local peritoneal infection is required The drains are left in place for seven to ten days and then gradually removed permitting the cavity to granulate from below Aside from the increased risk in such cases there is a prolonged convalescence due to the fact that the wound must heal by secondary intention and a small *draining fistula may persist for some time*

The mortality in appendicitis with perforation and abscess formation formerly varied from 5 to 30 per cent With practice of pre and post operative injections of penicillin (p 106) and of streptomycin (p 103) the mortality rate has been reduced appreciably

Occasionally in patients who are gravely ill with an appendiceal abscess it may be *impossible to remove the appendix In such cases* simple drainage of the abscess combined antibiotic streptomycin and penicillin therapy will ordinarily cause subsidence of acute symptoms At a subsequent date the appendix can be removed with little risk

Appendicitis with Generalized Peritonitis—Surgery in appendicitis with diffuse peritonitis is associated with grave risk In general the prognosis

Appendicitis in Infancy —The diagnosis of appendicitis in infancy is made more difficult by the fact that the child is unable to report the subjective manifestations Under these circumstances the physician is dependent upon physical signs of which the most important is the presence of *localized muscular rigidity in the right lower quadrant* *Persistent vomiting* is highly suggestive especially if there is noted an associated fever and leukocytosis The appearance of the mass representing an appendiceal abscess points to the definitive diagnosis but the practitioner attempts to recognize the condition before this complication is encountered

Appendicitis in Pregnancy —Appendicitis in pregnancy gives rise to *diagnostic and technical difficulties* *The infected organ is hidden beneath* the enlarged uterus obscuring the physical signs which may be interpreted as the normal discomfort of the gravidity The most reliable findings are those obtained by rectal examination If these are definitive and persistent particularly with associated fever and leukocytosis operative interference is not delayed since neglect may lead to the death of mother and child *Contrary to the general belief laparotomy has but little increased risk* and does not cause miscarriage or premature labor

Diagnosis —The diagnosis of acute appendicitis is a clinical discipline in its early stages when operative interference is safe and simple The practitioner arrives at an inferential conclusion and backs his judgment by immediate laparotomy It is far better to remove a large number of *normal appendices than to neglect one at the forfeit of a human life*

Many intra abdominal lesions and an occasional supradiaphragmatic condition simulate the syndrome of acute appendicitis Simple *gastro enterocolitis* (p 1878) is easily recognized if there is a diarrhea independent of purging Muscle rigidity should not be present but there may be an associated elevation of temperature and a leukocytosis *Cholecystitis* (p 2009) often simulates an appendicitis although characteristically pain and tenderness are located higher in the cavity

In *female* children *pyelitis* (p 2303) is recognized by the presence of pus in the catheterized urine specimen but the astute practitioner recalls that the two conditions may coexist Pyelitis is apt to be associated with chills and a more considerable elevation of temperature but the same marked constitutional symptoms occur with the diffuse peritonitis that occasionally complicates appendiceal infection

In older patients *calculous disease of the kidneys* (p 2314) gives rise to confusion When there is doubt a cystoscopy is indicated and the obstruction is demonstrable by ureteral catheterization Pelvic inflammatory disease especially *salpingitis* (p 2608) may closely resemble appendiceal infection In the former other evidences of gonorrheal infection or a history of an illegal abortion may be obtained rectovaginal examinations reveal the indurated mass in the fornix and the sedimentation time is apt to be very rapid The two conditions may coexist however and when this is so an exploratory laparotomy is necessary to settle the diagnosis

Mesenteric lymphadenitis (p 2730) is indistinguishable from an acute appendicitis except by operative findings Since each of these conditions responds favorably to appendectomy the indications and treatment are alike

The condition is recognized at operation at which time the involved structure is excised If the vermiform appendix is within the field it is removed as a prophylactic measure

MESENTERIC LYMPHADENITIS

Inflammation of the mesenteric lymph glands may be of *tuberculous* or *nontuberculous origin* The latter is usually a hematogenous infection

DIFFERENTIAL DIAGNOSIS OF

Pain in the Umbilical Region

Periumbilical discomfort is frequently a manifestation of acute appendicitis or of some congenital defect associated with the cord. The diagnosis is a clinical discipline in either event since laboratory investigations are of no avail.

	DIAGNOSTIC FEATURES
Omphalitis	Inflammation of the cord structures, particularly in infancy Note localized redness, swelling and discharge (p 2785)
Persistence of Urachus	With reflux of urine particularly with bladder distention and inflammation Consider laparotomy (p 2287)
Inflammation of Meckel s Diverticulum	With evidences of local inflammation Occasionally demonstrable by x rays with barium but usually requiring exploratory laparotomy (p 1864)
Acute Appendicitis	With later shifting of pain and tenderness to right lower quadrant. Urgent indication for laparotomy
Acute Intestinal Obstruction	May be due to intussusception or volvulus former more common in infancy and latter in adult life Attempt gentle reduction with barium enema and manipulation under vision (p 1873) Consider laparotomy if efforts are unsuccessful
Rupture of Graafian Follicle	Dysovulation between 10th and 16th days following initiation of previous menstrual period Consider laparotomy (p 2528)
Spasmosis	May be associated with hypersthenic gastrointestinal neurosis dietary indiscretion, food poisoning enterocolitis or plumbism Simulation of acute appendicitis may require diagnostic laparotomy (p 1846)

that follows an acute upper respiratory *infection* in a child or young adult The condition *cannot* be differentiated from an acute appendicitis (p 1881) and requires exploratory laparotomy

Mesenteric lymphadenitis of *tuberculous* origin represents a primary infection from drinking *unpasteurized* milk infected with the bovine strain (p 252) Caseation of the glands produces a right side itis indistinguishable from an appendicitis A preoperative *diagnosis* is made occasionally when a scout *film* reveals the shadows of a calcified lesion

depends upon the duration of the peritonitis Thus if the peritonitis is of more than thirty six to forty eight hours duration the mortality rate rises steeply to 20 per cent If of less than twenty four hours duration the removal of the appendix and local drainage down to the appendiceal stump usually gives satisfactory results with a mortality which should not exceed 10 per cent Combined therapy with streptomycin and penicillin has greatly reduced morbidity and fatality Anti infective therapy is supplemented by the use of an indwelling stomach tube and intravenous fluids

DIFFERENTIAL DIAGNOSIS OF

Swellings and Tumors of the Right Lower Quadrant

The frequency of appendiceal abscess directs the suspicion of the practitioner to the possibility of the existence of this condition under any circumstance Exploration, however often reveals the presence of other pathologic conditions involving the ileocecal region or the female adnexa

SITE OR TYPE	DIAGNOSTIC FEATURES
Appendiceal	Inflammation or abscess of appendix Note localized pain and tenderness confirmed by rectal examination (p 1881) Prepare for laparotomy
Cecal	Spasm inflammation or neoplasm of cecum Confirm by barium enema and multiple examinations of the stool for occult blood (p 3728) Prepare for exploratory laparotomy
Ileal	*Regional ileitis May be associated* with persistent fistula Confirm by barium meal and exploratory laparotomy (p 1851)
Gynecologic	*Ovarian cyst or neoplasm* Tubo-ovarian abscess or tubal pregnancy Rapid sedimentation time with inflammation Urinary test for pregnancy in ectopic gravidity (p 2657) Consider exploratory laparotomy
Intussusception	Acute *evidences of* intestinal obstruction in infancy and childhood Palpable mass confirmed by gentle barium enema (p 1876) Prepare for laparotomy
Peritoneal	Localized abscess
Renal	Ptosed or enlarged kidney Get urogram and perform cystoscopy (p 2248)

EPIPLOITIS

Most adults have as many as one hundred *appendices epiploicae* which are localized pedunculated overgrowths of the subserous fat of the mesentery They are most numerous in the transverse and pelvic colons and are arranged in rows along the anterior and posterior muscular bands *The integrity* of the appendices epiploicae occasionally becomes compromised due to torsion or infection Under these circumstances interference with the blood supply causes *gangrene* and *manifestations of localized or diffuse peritonitis* (p 1923) appear

The condition is recognized at operation at which time the involved structure is excised If the vermiform appendix is within the field it is removed as a prophylactic measure

MESENTERIC LYMPHADENITIS

Inflammation of the mesenteric lymph glands may be of *tuberculous or nontuberculous origin* The latter *is usually a hematogenous infection*

DIFFERENTIAL DIAGNOSIS OF

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Mesenteric lymphadenitis of tuberculous origin *represents a* primary infection from drinking unpasteurized milk infected with the bovine strain (p 252) Caseation of the glands produces a right side itis indistinguishable from an appendicitis *A preoperative diagnosis is made* occasionally when a scout film reveals the shadows of a calcified lesion

The resemblance of mesenteric lymphadenitis to appendicitis requires that surgical intervention be advised At worst an unnecessary procedure is accomplished and a prophylactic appendectomy performed The risk of this error is negligible in comparison with the complications of an unrecognized appendiceal lesion

NEOPLASMS

BENIGN TUMORS OF THE INTESTINE

Benign tumors may be present in the small or large bowel *Fibromas lipomas neurofibromas hemangiomas adenomas* and *fibro adenomas* have been described as clinical rarities The growth may be single or multiple and is usually asymptomatic unless there occur hemorrhages recurrent episodes of intussusception or intestinal obstruction Under any of these circumstances the diagnosis is made at operation and the treatment is by excision

Polyps —*Intestinal polyps* may be *congenital under which circumstances* they are multiple The *acquired polyps* occur as the result of a chronic inflammatory process such as ulcerative colitis (p 1856) Polyps are prone to ulcerate and bleed They may undergo malignant degeneration Solitary polyps are occasionally found in the rectum where they are easily removed through the operating proctoscope (p 1907)

CANCER OF THE RIGHT HALF OF THE COLON

Cancers of the right half of the colon which is a portion of the fore gut are usually large, ulcerating medullary *adenocarcinomas* they occur most often in the fifth and sixth decades and are more frequent in males than females they may take their origin from a preexistent adenomatous polyp and may be multiple The fungating adenocarcinomas of the right half of the colon do not tend to produce obstruction they rarely encircle the bowel but grow outward from the lumen and cause *penetration* and *perforation* involving adjacent structures they bleed slowly and give rise to an insidious anemia

Clinical Manifestations —The most frequent complaint in carcinoma of the right half of the colon is generalized *weakness* and *pallor* with the development of a *secondary anemia* Often the patient notes recurrent bouts of a *mucoid diarrhea* alternating with *constipation* With the diarrhea there may be *abdominal cramps* and *borborygmi* There is progressive *loss of weight* and by the time the patient seeks advice a mass is clearly palpable the stool contains gross or occult *blood* and *radiography* reveals an *extensive filling defect*

Complications —See page 1891

Treatment —In carcinomas of the *cecum ascending colon and hepatic flexure (right portion of bowel)* surgical treatment is mandatory as soon as the patient s condition has been improved by preoperative preparations (p 1834) The first stage consists of an anastomosis of the terminal ileum to the transverse or sigmoid colon (ileocolostomy) The ileum is then divided distal to the anastomosis After a lapse of two or three weeks the entire half of the colon and the stump of the ileum are resected

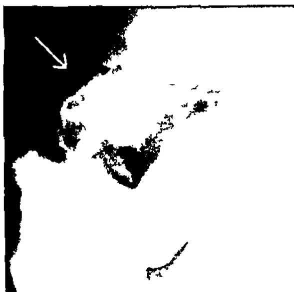


Fig 427—Carcinoma of the ascending colon

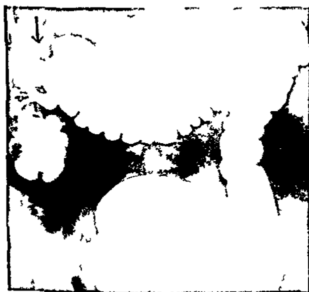


Fig 428—Carcinoma of the hepatic flexure not clearly seen at this time

a preliminary intestinal intubation having been instituted before the second stage

Buckstein Clinical Roentgenology of the Alimentary Tract



Fig 429 —Carcinoma at the splenic flexure *

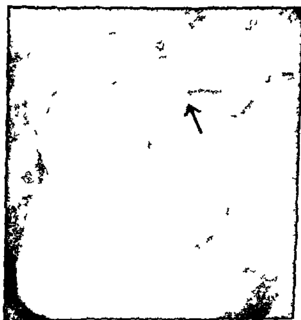


Fig 430 —Appearance produced by an annular scirrhous type of carcinoma of the sigmoid

* Buckstein Clinical Roentgenology of the Alimentary Tract

CANCER OF THE LEFT HALF OF THE COLON

The left half of the colon is derived from the hindgut Malignancies in this location are usually of the *annular scirrhous variety* these lesions encircle the gut and produce *intestinal obstruction* (p 1873) and brisk and sudden *hemorrhage*

Clinical Manifestations.—The clinical manifestations of malignancy of the left half of the colon consist of episodes of acute subacute or chronic *intestinal* obstruction at which time the patient notes *pain distention borborygmi nausea vomiting* and *fever* The observant patient states that the stool has changed in character and is narrow or *ribbon like* A frequent complaint is a failure to feel completely evacuated though there is a daily bowel movement *Red blood* may appear mixed with the stool or on the toilet paper as a herald manifestation In contrast to the patient who has a malignancy in the right half of the bowel there may be very little loss of weight or strength and a relatively normal blood count

Abdominal palpation reveals the hard *mass* which also may be visible by sigmoidoscopy (p 1907) and palpable by rectal examination Occasionally the first evidence of the growth is a sudden exsanguinating *hemorrhage*

Complications.—Malignant processes of the large bowel cause local complications of *perforation penetration* and *hemorrhage* At times they are diagnosed only when the attention of the physician is drawn to the abdomen as the result of the finding of metastases in the *liver bones* or *lungs Secondary anemias* occur more often in the fungating adenocarcinomas of the right colon

Treatment.—The treatment of carcinoma of the colon is surgical after meticulous preoperative preparation (p 1834)

Carcinomas of the *left half of the colon* and the distal sigmoid are best resected by some modification of the technic of obstructive resection (p 1836) A segment of colon is removed and a double barreled colostomy is constructed For three to six days following operation the loops of the colostomy are occluded by clamps to permit early uncontaminated wound healing This procedure may or may not be preceded or accompanied by a cecostomy for decompression At a later stage the spur between the lips of the colostomy is divided by a crushing clamp the bowel is then clo ed by an extraperitoneal procedure

Lesions of the *lower sigmoid* are treated by a preliminary diverting colostomy followed by resection and anastomosis as indicated above in rectal lesions abdominoperineal resection is performed with establishment of a permanent colostomy (p 1836)

CARINOCIDS

The carcinoid is a locally invasive tumor originating from the nerve elements about the intestines This neoplasm is observed relatively rarely and is diagnosed usually only at operation *Carcinoma of the appendix* is very rare and is discovered on operation performed to investigate a mass in the right lower quadrant Treatment is surgical (p 1834)

INTESTINAL INFESTATIONS

A large number of protozoa inhabit the intestinal tract of man The vast majority are harmless *commensals* (p 146) including *E coli E nana*

L butschlii fragilis and *Trichomonas hominis* These assume importance only because they may be mistaken for the *Endamoeba histolytica* the causative agent in amebic dysentery described in the chapter on the general systemic infections (p 523)

Occupying a position intermediate between the commensals and the definitive pathogens are *Giardia lamblia* and *Balantidium coli* These organisms are capable of setting up the local inflammatory processes of *giardiasis* and *balantidiasis*

GIARDIASIS

The most frequently observed flagellate that inhabits the intestinal tract of man is the Giardia lamblia The organism appears as the trophozoite or in a cystic form The *trophozoite* is pear shaped possesses eight flagella and moves in a rapid jerky fashion The *cysts* are smaller oval bodies surrounded by refractile double walls Trophozoites are most numerous in the duodenum but occur throughout the small intestine and



Fig 431 —Vegetative form of *Giardia lamblia* in feces photomicrograph (about × 800) *



Fig 432 —Photomicrograph of *Balantidium coli* in feces (about × 500) *

are recognized in fluid stools The cysts are found in the ileum and colon and are present in formed stools

Giardia lamblia is transmitted to man through the ingestion of food or water contaminated by fecal material passed by other infected individuals Its method of transmission is similar to that of the *E histolytica* (p 525) It is estimated that 5 to 15 per cent of children *under the age* of ten harbor the giardia in their intestinal tracts When these youngsters develop an enterocolitis (p 1872) the organisms are readily identified by microscopic examination of the stool specimen It has not been definitively established that the giardia are pathogenic *since they may be mere chance findings in an inflammatory* process caused by some other organism

Treatment —Giardiasis requires treatment when the symptoms of dysentery are persistent and no other causative factor can be demonstrated The drugs employed include *carbarsone* and *chiniofon* used in the same

* Todd and Sanford Clinical Diagnosis by Laboratory Methods

manner as in the treatment of *amebiasis* (p 597) If the giardia is resistant to therapy atabrine has been recommended as in the treatment of *malaria* (p 507)

BALANTIDIASIS

The Balantidium coli frequently produces a local *enterocolitis* (p 1872) in inhabitants of the United States as well as the countries of Central and South America The domestic *pig* serves as the normal host for these infusoria and is the reservoir from which human infection is derived

Balantidium coli is a relatively large organism ovoid in form with a funnel shaped mouth at the more pointed anterior end Its surface is covered with a dense cuticle marked with longitudinal lines in which cilia are set at regular intervals The *macronucleus* is large and kidney shaped while the *micronucleus* is small and usually situated within the indentation of the macronucleus Contractile vacuoles are present in the cytoplasm as well as red blood corpuscles and other cells that may be present in the near vicinity

Fortunately the mere ingestion of the encysted organism is not sufficient to cause infection Obviously some accessory factor must be required else balantidiasis would be of much more common occurrence The majority of patients who harbor the *B coli* have no symptoms Under circumstances not clearly understood the tissues may be invaded giving rise to a *diarrhea* (p 1840) with blood and mucus in the stool The *diagnosis* is readily established by identifying the organism though it must be borne in mind that the balantidium may be a commensal in an individual whose colitis is due to some other organism such as the *Endamoeba histolytica* (p 595)

Treatment—Ridding the stool of *B coli* requires the use of potent agencies such as *tryparsamide* (p 120) *emetine* (p 527) or *Oil of Chenopodium* The toxicity of these preparations seems out of all proportion to the relative mildness of the infection It would seem the greater part of wisdom to employ symptomatic therapy unless the clinical manifestations are unduly severe or persistent

INTESTINAL HELMINTHIASIS

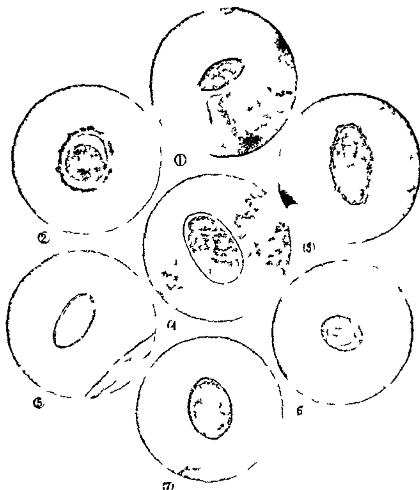
The present material treats of helminthic invasions of the intestinal tract *systemic helminthic diseases* are discussed in the Chapter on Systemic Infections by Protozoa and Helminthes (p 506) *hepatic* and *pulmonary distomiases* are taken up respectively with disturbances of the liver (p 1983) and lungs (p 2213) tissue roundworms (filaria) and their cutaneous manifestations appear in the Section on The Tegumentary System (p 3321)

Varieties—The intestinal helminthic diseases are classified as follows

- Fluke Infestations (Distomiasis)
- Flatworm or Tapeworm Infestations (Teniasis)
- Roundworm Infestations
  - Oxyuriasis
  - Uncinariasis
  - Strongyloidiasis
  - Ascariasis
  - Trichiuriasis

Diagnosis —The diagnosis of infestation is established by the finding of the worm or its ova in stool specimens (p 3731)

Treatment with Anthelmintics —The anthelmintics are designed to rid the host of parasites that have taken up an existence within the lumen of the gastro intestinal tract *vermifuges* remove the worm and *vermicides* destroy the invader An anthelmintic sufficiently potent to kill the invad



Figs 433–434 —Ova which may be found in the feces showing comparative size (photographs × 250) 1 *Trichuris trichiura* (whip-worm) 2 *Ascaris lumbricoides* (round worm) fertilized 3 *Ascaris lumbricoides* unfertilized 4 *Necator americanus* (hookworm) four-cell stage 5 *Enterobius vermicularis* (pin worm) 6 *Hymenolepis nana* (dwarf tapeworm) 7 *Diphyllobothrium latum* (fish tapeworm) the edge of the lid being out of focus

ing worm is potentially toxic for the host Hence it is highly important to employ anthelmintics that are not absorbed and that may be rapidly removed from the intestinal tract The practitioner is urged to use the safer preparations of hexylresorcinol tetrachlorethylene gentian violet and aspidium pelletierine chenopodium santonin thymol carbon tetrachloride and betanaphthol are reserved for treatment failures

Todd and Sanford Clinical Diagnosis by Laboratory Methods

Hexylresorcinol—For routine use by the practitioner hexylresorcinol is the drug of choice in the treatment of *ascaris hookworm* and *trichocephalus infestations* As Crystoids or Caprokol it is marketed in hard gelatin capsules containing 0 2 gm (3 grains) The average adult dose is 5 capsules (1 gm or 15 grains) Children below the age of six may take 3 capsules of 0 6 gm The capsules must be swallowed whole during the fasting stage or digestion

Following the administration of the drug which can be given in a single dose no food is taken for five hours At the end of two to four hours a saline purge is administered Hexylresorcinol owes its efficacy chiefly to its antiseptic action the drug is a local irritant but causes *little systemic toxicity* The course can be repeated several times without danger

Hexylresorcinol is given also in a retention enema of 1 1000 solution of bicarbonate of soda preceded by an ordinary water enema to evacuate feces from the large bowel

Tetrachlorethylene—Tetrachlorethylene is used chiefly against *hookworm it possesses little or no toxicity and is preferred to carbon tetra* chloride and thymol

Tetrachlorethylene N F is a colorless fluid it is prescribed in soft gelatin capsules each containing a dose of 1 cc The average dose is 3 cc The dose for children is 0 2 cc per year of age The patient is placed on a full diet for several days before the drug is administered alcohol and fats are banned saline purges are given the night before and two hours after the administration of the anthelmintic The drug may be repeated in two weeks Precautions are taken to discard capsules that may have been exposed to air since *phosgene* may be formed by decomposition

Gentian Violet—Gentian Violet N.N.R is marketed in coated tablets containing 30 mg (½ grain) It is an antiseptic dye used as an anthelmintic in the treatment of *Strongyloides stercoralis* and *oxyuris* infestations Two of the tablets (0 06 gm) are given three times daily for seventeen days In obstinate cases 25 cc of a 1 per cent solution may be given directly into the duodenum Excessive doses produce nausea and vomiting but there are no other systemic effects

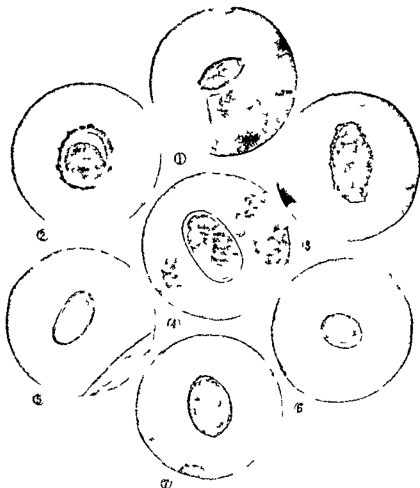
Aspidium (*Male Fern*) —Aspidium is the anthelmintic of choice in the treatment of infestation with *tapeworms* The official preparation is *Oleoresin of Aspidium* a thick dark green unpleasant tasting fluid The drug is best dispensed in capsules each containing 0 6 cc (10 minims) The total dose consists of 2 capsules (1 2 cc) every thirty minutes for three doses or 3 6 cc

Aspidium is administered under strictly regulated precautions The patient is placed on a *fat free diet* for two days prior to the administration of the drug On the second day luncheon and supper are omitted but fluids are taken liberally The evening before *magnesium sulfate* is administered Oily cathartics such as castor oil are avoided since they increase absorption

The morning following the saline catharsis *aspidium* is given in three divided doses a half hour apart Two hours after the last dose the patient again takes *magnesium sulfate* for the purpose of ridding the intestine of parasite and drug Two hours after the saline the patient receives a copious *soapsuds enema* Stool and enema returns are strained and care

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Todd and Sanford Clinical Diagnosis by Laboratory Methods

dose is usually given with calomel or a saline such as magnesium sulfate If calomel is employed the santonin calomel combination should be followed in two to four hours by a saline Castor oil favors the absorption of santonin hence it is strictly contraindicated The drug is best given following the breakfast or evening meal since absorption and general symptoms are more apt to occur if the stomach is empty when the anthelmintic is administered

The special *toxicology* of santonin involves color vision hearing smell and taste Objects may first appear blue and then yellow later the patient complains of impairment of hearing headache vomiting abdominal pains and diarrhea epileptiform convulsions may occur Because of the violence of santonin poisoning probatory doses are suggested before administering the full anthelmintic amount

Thymol—Thymol is useful in the treatment of *hookworm* but it has been replaced by the less toxic *carbon tetrachloride* (p 1897) and *tetrachlorethylene* (p 1895) The official thymol occurs in large colorless prisms It is most conveniently administered in gelatin capsules each containing 0 3 gm (5 grains) The total daily dose should not exceed 4 gm for men 3 gm for women The total daily dose is divided into two or three equal portions taken at intervals of one or two hours For children less than five years of age two capsules or 0 6 gm are administered Up to ten years of age 3 capsules are given

The patient is placed on a full diet before the administration of thymol alcohol and fat are prohibited A *saline purge* is administered preceding the administration of the drug and following the last capsule Treatment may be repeated at weekly intervals

Thymol is an intense local irritant Absorption which is favored by the presence of alcohol and fat may cause convulsions from stimulation of the central nervous system with subsequent depression and respiratory and circulatory failure These hazards have led to the substitution of safer anthelmintics

Carbon Tetrachloride—Carbon tetrachloride is of chief value in the treatment of *hookworm infestations* Despite its efficiency and economy its toxicity has led to the substitution of *tetrachlorethylene* (p 1895)

Carbon tetrachloride U S P is a volatile colorless liquid resembling chloroform It is administered in gelatin capsules the adult dose is 3 cc and the average dose for children is 0 2 cc per year of age up to the adult amount

Preceding the administration of the drug the patient is placed on a high carbohydrate and low fat diet A light meal is taken before the dose of the drug and a mild laxative is prescribed at bedtime In the morning the capsules are taken on an empty stomach two or three hours later magnesium sulfate is given The anthelmintic course may be repeated in three weeks if necessary

Carbon tetrachloride is an intense local irritant After absorption which is augmented by alcohol it produces a chloroform like effect depressing nervous system and circulation and causing a severe toxic hepatitis

Betanaphthol—Betanaphthol U S P is a buff colored powder used to combat hookworm infestations The usual adult dose is 4 gm divided into two equal doses followed by a saline purge

fully examined for identification of the head of the worm If this is not found therapy has not been successful and must be repeated after the lapse of several days or a week

The *toxicology* of aspidium is local and distant Locally the drug is an intense irritant If given undiluted it may cause nausea vomiting and bloody diarrhea It is for this reason that fluids are prescribed liberally two days previous to and on the day of the administration of the anthelmintic

The successful anthelmintic action of aspidium is due to its depression of the smooth muscle of the worm This paralyzant effect permits the worm to be removed from the intestinal tract After absorption aspidium produces a similar effect upon smooth and cardiac muscles of the host and strongly stimulates the spinal cord The toxic symptoms exhibited by the host are determined by individual idiosyncrasy they may include convulsions liver atrophy cardiac depression and collapse nausea vomiting gastro enteritis with abdominal pain and bloody diarrhea respiratory depression and occasionally death

Because of the dangers of aspidium administration the drug should not be used in weak individuals those with gastro intestinal disease patients who suffer from cardiac hepatic or renal lesions or during pregnancy

Pelletierine —The increased toxicity of pelletierine makes it inferior to aspidium as an anthelmintic It possesses no advantages

Pelletierine Tannate U S P is obtained from the bark of the pomegranate It has the same usages and the same methods of administration as aspidium It is given in a single dose of 0 25 gm (4 grains) followed in thirty minutes by a saline cathartic

Oil of Chenopodium (American Worm Seed) —Oil of chenopodium is used in the treatment of infants with *hookworm roundworm* and *pinworm* infestations Because of its toxicity chenopodium has been largely replaced by the newer preparations particularly *tetrachlorethylene* (p 1895)

The official oil is a colorless or pale yellow liquid It has an unpleasant odor and a bitter burning taste It is administered in drop doses on granulated sugar or given in hard gelatin capsules The usual dose is 1.5 to 3 cc given in divided dosages in three portions ingested at hourly intervals

Prior to the use of the anthelmintic the patient is placed on a *high carbohydrate diet* for a few days The evening preceding the use of the drug a light supper is given followed by a purge with *magnesium sulfate* In the morning the patient receives a glass of milk and the chenopodium Two hours after the last dose a *second saline purge* is administered The course of treatment may be repeated every three to five days until all parasites have disappeared from the stool

Oil of chenopodium is an intense *local irritant* and may cause symptoms of inflammation of stomach or intestines After absorption the drug briefly stimulates and then markedly depresses the central nervous system simultaneously blood pressure falls and the patient may collapse

Santonin —Santonin is most effectively used in *ascaris* infestation The official Santonin U S P occurs as odorless colorless crystals slightly bitter to taste It is conveniently administered in capsules the adult dose being 0 06 to 0 18 gm (1 to 3 grains) and for children 0 001 gm per year of age The amount is given once daily for two or three consecutive days The

M yokogawai
China, Korea, Japan Formosa, Siberia, Dutch East Indies Russia Spain
E ilocanum
Philippines China Celebes

Life Cycles.—Intestinal flukes live in the small intestines and the immature eggs are passed in the feces In water the eggs mature and attack the *intermediate snail host* *Sporocysts* develop and *cercariae* escape from the snail and attach themselves to various plants where they become encysted Man becomes infected by eating the pods and bulbs of these aquatic specimens The cyst wall is digested in the duodenum and the *metacercaria* grow to maturity completing the cycle

Clinical Manifestations —The majority of infested patients have no significant clinical manifestations Those who suffer from intestinal distomiasis note a prolonged period of *asthenia* which is followed by an attack of *diarrhea* with *abdominal pain* Sooner or later, a generalized *edema* is noted affecting in order the abdominal cavity, the genitalia and the lower extremities The skin becomes harsh and dry the tongue is coated the temperature is subnormal

The association of diarrhea and edema is regarded as pathognomonic by physicians familiar with this affliction and the characteristic operculated eggs are readily demonstrable by microscopic examination of feces (p 3731)

Treatment —*Thymol* (p 1897) and *betanaphthol* have been reported as successful agents for the expulsion of the intestinal flukes more recently *carbon tetrachloride* (p 1897) has been recommended If these measures are unsuccessful the plan of treatment used in *hemic distomiasis* (p 537) must be employed using the antimony preparations Most experts prefer intramuscular injections of 7 per cent fuadin using 0 3 cc per 30 pounds of body weight as an initial probatory dose If there are no untoward effects the dose is increased to 0 75 cc per 30 pounds on the second day and 1 cc on the third fifth seventh ninth eleventh thirteenth fifteenth seventeenth and nineteenth days—but no more than 5 cc is permitted as a total daily dose The course may be repeated every one to four weeks until ova disappear from stools

Intestinal Teniasis (Tapeworm)

The intestinal tapeworms are observed with great frequency in man In the United States the commonest form of infestation is by the *beef tapeworm* (*Taenia saginata*) Less often disturbances are caused by the *pork tapeworm* (*Taenia solium*) or the *broad-fish tapeworm* (*Diphyllobothrium latum*)

Life Cycle —The life cycle of *T saginata* will be described since this is the most frequent form observed in the United States and well illustrates the general features of tapeworm existence

The adult *tapeworm* lives in the small intestine of man The terminal *proglottids* and linea segments are packed with mature eggs It is estimated that, at any given time each terminal segment may contain 124 000 ova and that each worm has an annual output approximating 594 000 000 eggs The terminal proglottids pass out with the feces Should they rupture eggs are set free and are recognized in the stool The excreta becomes strewn on the soil and the eggs are eaten by cattle grazing on grounds that have been polluted by human feces

In the intestines of the intermediate cattle host the embryo is freed by digestion of the shell, penetrates the intestinal wall and is picked up by the portal circulation It is carried

Betanaphthol is a powerful germicidal agent that often produces abdominal pain, nausea, vomiting, diarrhea and stimulation of the central nervous system followed by depression. It is toxic to both liver and kidney, hence it has been replaced in the treatment of hookworm by less toxic remedies.

TABLE 123.—THERAPEUTICS OF THE ANTHELMINTICS

Preparation	Preparatory Treatment	After Treatment	Preparation	Total Adult Dose	Childhood Dose	Indications
Hexylresorcinol (Caprokol Crystoids)	Saline purge previous evening	No food for 5 hours and saline purge after 2 hours	Capsules 0.2 gm.	1.0 gm. in single dose	0.8 gm.	Ascariasis, Hookworm, Trichocephalus, Tapeworm, Oxyuriasis, Trichuriasis
Tetrachlorethylene	Avoid fats and alcohol for 2 days. Saline purge on previous evening	Saline purge after 2 hours	Capsules 1.0 cc.	3.0 cc in single dose	0.2 cc. per year to adult dose	Hookworm, Ascariasis
Gentian violet	None	None	Tablets 0.03 gm.	0.06 gm. t.i.d. for 8 to 17 days	[illegible] gr. per year t.i.d. to adult dose	Strongyloides, Oxyuriasis
Aspidium	No fat or alcohol for several days. Saline purge on previous evening	Saline purge after 2 hours, followed by soapsuds enema	Oleoresin in capsules 0.6 cc.	2 capsules (1.2 cc.) every 30 minutes for 3 doses	1 drop per year to adult dose	Tapeworm
Pelletierine tannate	No fat or alcohol for several days. Saline purge on previous evening	Saline purge after 2 hours, followed by soapsuds enema	Capsules 0.25 gm.	0.25 gm.	Avoid	Tapeworm
Santonin	None	Saline purge after 2 to 4 hours	Capsules 0.06 gm.	0.18 gm. with calomel 0.12 gm. daily for 2 or 3 days	0.004 gm. per year to adult dose	Ascariasis
Thymol	No alcohol or fats for several days. Saline purge on previous evening	Saline purge after 2 hours	Capsules 0.3 gm.	4 gm. in 2 equal doses	0.6 to 0.9 gm.	Hookworm, Distomiasis
Carbon tetrachloride	High carbohydrate, low fat diet. Saline purge on previous evening	Saline purge after 2 hours	Capsules 1.0 cc.	3 cc.	0.2 cc. per year to adult dose	Hookworm
Betanaphthol	None	Saline purge after 2 hours	Capsules 1.0 gm.	4 gm. in 2 divided doses	1 gm.	Hookworm, Distomiasis
Phenothiazine	None	None	Capsules 1 gm.	1 gm. daily for 4 days	0.5 gm. daily for 6 days	Oxyuriasis

INTESTINAL DISTOMIASIS (FLUKES)

The intestinal flukes are rarely observed in the United States. The pathogens include *Fasciolopsis buski*, *Heterophyes heterophyes*, *Metagonimus yokogawai* and *Echinostoma ilocanum*.

Geographical Distribution.—The geographical distribution of the intestinal flukes as given by the United States Naval Medical School is as follows:

F. buski
China (Central, South), Indo China, Siam, Borneo, Sumatra, Malay Peninsula

H. heterophyes
Egypt, Palestine, China (Central, South), Japan, Formosa, Korea

Clinical Manifestations.—The clinical manifestations of infections with pork, beef and broad tapeworms are indistinguishable. The patient complains of vague *abdominal pressure* and discomfort, with interpolated episodes of *colic*. The *appetite* is *irregular* and may be *capricious*. The incidence of morbid hunger has probably been exaggerated, since many patients



Fig. 4 6.—Echinococcus cysts in the liver. Daughter cysts with chitinous wall are dislocated from the outer wall.

complain of nausea and vomiting. The bowels may be constipated, but there are occasionally episodes of *diarrhea*. During the latter segments of the worm may be expelled, leading to the diagnosis. At times the bulk of the worm produces *intestinal obstruction* (p. 1873). Most often the diagnosis of tapeworm infestation results from a routine survey in an area where it is known that the disease is common.

MacCallum: *Textbook of Pathology*.

then to the peripheral circulation and settles in the muscles particularly the pterygoid tenderloin and heart where it develops into a *Cysticercus bovis* The cycle is completed by the ingestion of raw or insufficiently cooked beef which contains the cysticerci The *scolex*

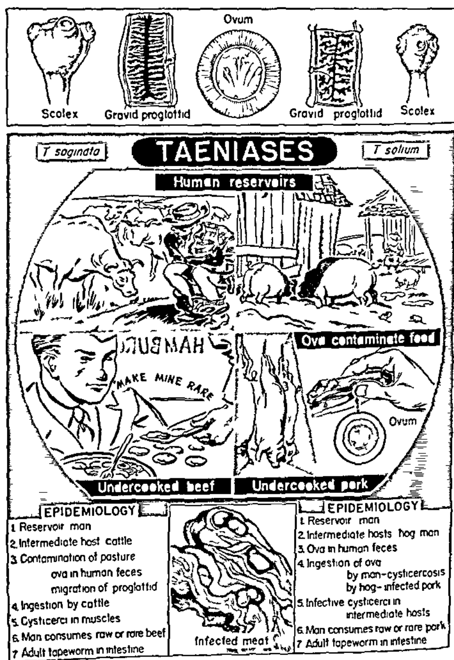


Fig 435 —Epidemiology of the taeniases

is *liberated* by digestion attaches itself to the intestinal wall and the *proglottids* begin to form The adult requires eight to ten weeks to reach maturity within the human host and then may live for twenty years or more

* Mackie-Hunter Worth, Manual of Tropical Medicine

down on the perianal skin with its adhesive surface applied to the integument Fecal particles epithelial cells and ova cling to the surface which is then placed lengthwise on a microscope slide smoothed down and examined with the 16-millimeter objective

Other than *pruritus ani* and consequent *restlessness* and *irritability* pinworms cause no difficulty

Treatment—Treatment is most safely accomplished by the use of *gentian violet* (p 1895) or *hexylresorcinol* (p 1895) Phenothiazine (nemazene) has been suggested in a dose of 1 gm daily for four days The anal

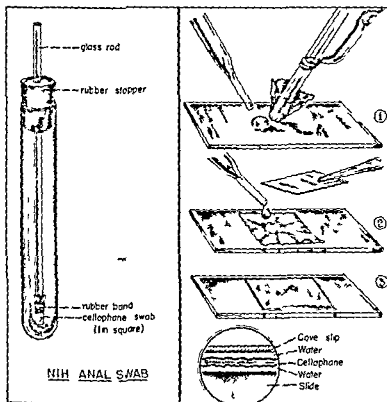


Fig 437—NIH anal swab (developed by the National Institute of Health) preparation for examination

regions are scrubbed with soap and water after which 2 per cent *ammoniated mercury* ointment is applied

UNCINARIASIS

(Hookworm Disease Ancylostomiasis Miner s Anemia Tunnel Worker s Anemia Tropical or Egyptian Chlorosis)

Hookworm disease is common in Southern Europe North Africa China Japan Southern United States the northern parts of South America Cen

In addition to the intestinal disturbances a severe *hyperchromic anemia* (p 1077) may develop particularly with the broad fish tapeworm infestation

Echinococcosis (Hydatid Disease)

Echinococcosis differs from other tapeworm infections in that huge *cysts* are formed usually in the *liver* The oncosphere or embryo which invades the tissues undergoes central liquefaction and grows to a considerable size eventually producing *daughter cysts* Hydatid cysts are most frequently observed in the liver but they may also be noted in the lungs or pleura The condition causes few symptoms other than a sense of heaviness in the region of the affliction and the appearance of a tumor

The patient s general condition is not impaired and the disproportion between the size of the tumor and the well being of the subject often suggests the diagnosis which is confirmed by demonstration of the *scolices* or *hooklets* in material obtained by aspiration A *complement fixation test* and a *skin reaction* are available and are in a period of experimental test

Diagnosis —The diagnosis of tapeworm infestation is established by the finding of ova and the proglottids in the stool specimen (p 3721)

Treatment —The treatment of intestinal tapeworm infestations requires the administration of *aspidium* (p 1895) *or hexylresorcinol* (p 1895)

Intestinal Infestations by Roundworms

The majority of the roundworms which infest man do not possess organs of attachment Only the *trichinella* actually invades human tissue and produces systemic symptoms as elsewhere described (p 530) The remaining members of this family are limited in their scope but are very commonly encountered In the United States the most frequent infestation is with the *oxyuris* (threadworm pinworm seatworm) Of greater medical importance is *hookworm disease* due to the *Ancylostoma duodenale* and the *Necator Americanus* *Ascariasis* is almost uniformly observed in inhabitants of the Pacific Islands

OXYURIASIS (PINWORM SEATWORM)

The *Oxyuris vermicularis* is the most common helminth observed in the United States Its *life cycle* is the essence of simplicity since there is no need for an intermediate host or a suitable soil for embryonation of the eggs When deposited each egg contains a larva that is ready to infect man its one and only host The deposition of the egg around the anus produces *itching* With scratching of the region the eggs adhere to the fingers from which they are transferred to the mouth thus completing the cycle

The female oxyuris is about 10 mm in length and contains two uteri which average more than 1000 eggs The male is 4 mm in length and the eggs are ovoid with a characteristic flattening on one side The shell is transparent and consists of an outer albuminous layer which causes the egg to adhere to the skin and an inner embryonic membrane See Fig 433

An ingenious method of demonstrating the parasite has been devised by Graham A piece of Scotch cellulose tape about 8 cm long is patted

egg has a well developed digestive tract It feeds voraciously for about three days and then moults On the fifth to eighth day the larva becomes *filariform* It develops in warm moist aerated soil where it becomes capable of penetrating the skin usually of the soles of the feet of barefoot persons by which mechanism it infects a new host

The *filariform larvae* reach the blood and lymph vessels and are carried through the right heart to the lungs Here they break into the alveoli and are transported up the bronchi and trachea and then down the esophagus into the stomach and small intestines It is in this last site that they develop into the adult form

Clinical Manifestations —Hookworm disease is frequently asymptomatic The initial symptom at the site of entry may be the appearance of the ground itch in barefoot persons

When the worms have become disseminated the patient develops a *secondary anemia* with a slight or moderate *eosinophilia* At this time *lassitude fatigue weakness* and *pallor* are noted Secondary metabolic disturbances particularly the *avitaminoses* are superimposed producing *edema stomatitis glossitis* and *peripheral neuropathies* Particularly characteristic complaints are *somnolence* and *lethargy* Children manifest *retarded development* and *pica*

The anemia may be so severe that the hemoglobin reading is reduced to 15 or 20 per cent and the red cells fall as low as 1 000 000 per cubic millimeter The color index is always low *Cardiac dilatation* and *hemic murmurs* are observed in the more severe afflictions

Diagnosis —The diagnosis of hookworm disease is made by finding the eggs or the worms in the *stool* (p 3721)

Treatment —The cure of hookworm disease is most effectively accomplished by the use of *tetrachlorethylene* (p 1895) which has replaced more toxic preparations such as *thymol* (p 1897) *carbon tetrachloride* (p 1897) and *oil of chenopodium* (p 1896)

An alternative vermicide is *hexylresorcinol* (p 1895) given in a single dose of 1 gm (15 grains) in the morning Food is avoided for four hours at the end of which time a saline purge is administered

In addition to the treatment of the infestation the patient with hookworm disease should be given a hematinic and supplementary doses of available vitamins

The *prevention* of hookworm disease requires that shoes be worn If ground itch develops the area is treated by freezing with dry ice for a minute or the application for twenty four hours of a pledget of cotton saturated with *ethyl acetate*

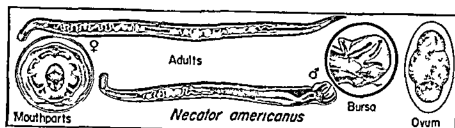
STRONGYLOIDIASIS (COCHIN CHINA DIARRHEA)

The *Strongyloides stercoralis* is an intestinal roundworm whose life cycle parallels that of the hookworm (p 1904) The important difference is the fact that the eggs are laid and hatched in the mucosa of the intestines and their larvae are passed in the feces

The diagnosis is usually made through the recognition of the rhabditiform larvae

The clinical manifestations and treatment of these infestations are the same as for hookworm disease *Gentian Violet* is the safest of the effectual vermicides (p 1895)

tral America the Caribbean Islands South Asia and Polynesia Of soldiers in the United States Army 16 per cent of those recruited from southern states harbored the organism

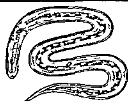


HOOKWORM

Anemia — Cachexia

Eggs passed in feces

Penetration of skin by larvae



EPIDEMIOLOGY

1 Fecal contamination of soil
2 Rhabditiform larvae in soil
3 Filariform larvae on soil
4 Penetration of exposed skin
5 Migration of larvae
6 Localization small intestine
7 Feeding on blood of host
8 Ova passed in stool



Fig 438 —Epidemiology of hookworm disease *

Life Cycle —The hookworms affix themselves to the mucous membrane of the small intestines feeding on the blood and lymph of their host The female lays 10 000 to 20 000 eggs a day and the span of life is three to eight years The larva which hatches out of the

* Mackie Hunter Worth Manual of Tropical Medicine

CHAPTER 94

THE RECTUM AND ANUS METHODS OF EXAMINATION AND TREATMENT CLINICAL DISTURBANCES

MAN and domestic animal are trained to repress the defecation reflex in order to preserve the "decencies of life The resultant rectal constipation leads to the widespread use of cathartics and enemas supplemented by squeezing efforts to expel the inspissated fecal mass Further trauma is inflicted by the vigorous friction of rough toilet paper the net result is the universal complaint of rear-end misery

ANATOMIC REVIEW

See p 3565

ANOSCOPY PROCTOSCOPY AND SIGMOIDOSCOPY

The physician who purchases an electrodiagnostic set may with great facility perform anoscopy procto copy and sigmoidoscopy The rheostat set serves as the better source of illumination (p 3588)

The short *anoscope* or *proctoscope* is easily passed with the patient in the knee-chest position The handle containing the source of illumination is provided with a glass window which magnifies To obtain specimens or perform local therapy the window can be removed Laterally the window has an outlet which permits attachment of an inflation bulb

After the anal canal has been entered and inspected it is not a difficult matter to insert the tube an additional few inches and view the lower sigmoid The appearance of the mucous membrane is noted Abnormalities particularly those suggesting *ulceration* and *neoplasm* may be referred to the specialist *Smears* and *cultures* may be taken from moist lesions *Biopsies* are obtainable from redundant tissue

The *sigmoidoscope* must be passed more cautiously Introduction is gently accomplished along the rectosigmoid lumen It is not difficult for the

ASCARIASIS

The *Ascaris lumbricoides* causes infestation of humans without any intermediate host The adult worms live in the small intestine and unsegmented noninfective eggs are passed in the feces Under favorable soil conditions the egg *embryonates* and develops a coiled *rhabditoid larva* which moults once and then becomes infective The cycle is completed when man *swallows the mature eggs which* pass through the stomach to hatch in the small intestine The larvae burrow into the intestinal wall and are carried to the lungs through the right heart In the lungs the larvae break into the alveoli where they moult twice and then migrate via the bronchi esophagus and stomach back to the small intestines where they complete their development in about two months

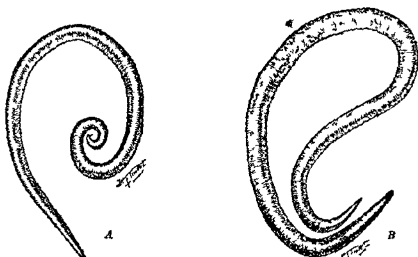


Fig 489 —The common roundworm *Ascaris lumbricoides* natural size *A* Male *B* female

Ascariasis is *treated* with *hexylresorcinol* (p 1895) and *tetrachlorethylene* (p 1895) as in uncinariasis (p 1905)

TRICHURIASIS (WHIPWORM)

The whipworm lives in the cecum Its unsegmented eggs are passed in the feces and embryonate in the soil Man swallows the eggs *which hatch* in the small intestine The larvae pass directly into the cecum where development continues to maturity

Infestations are usually asymptomatic and respond to the administration of *hexylresorcinol* (p 1895) or a preparation of the fresh sap of *Ficus laurifolia* a fig tree found in Colombia

* After Brumpt.

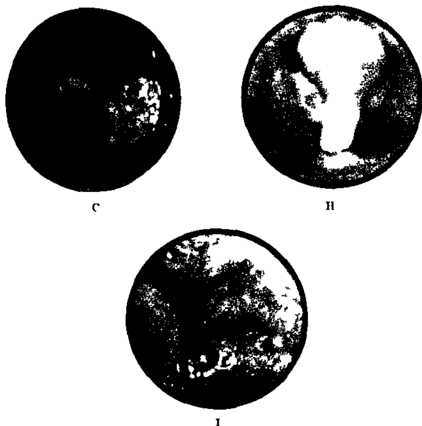


Fig 440 (*continued*) —Rectal diseases *G* A deep crypt behind sh htly hypertrophied pap llae *H* Papil of fib u structur with deep crypt *I* F ssure with senti l p l at right

practitioner to recognize hemorrhoids polyps neoplasms and ulcers of the various types The presence of *any lesion* warrants further investigation by a specialist *Spreads* (p 50) are to be examined for amebae and spirochetes *Tissue* should be sent to the *pathologist*

HYGIENE OF RECTUM AND ANUS

With rare exception afflictions of anus and rectum are due to errors in hygiene For many years the senior author has made it a point to instruct his patients in correct methods of caring for the lower end of the alimentary tract The result of this campaign has been virtually complete elimination of major difficulties The important principles in anorectal hygiene are correction of rectal constipation curbing the use of drastic cathartics avoidance of trauma during the unesthetic process of wiping with toilet paper and insistence upon replacement of extruded rectal mucosa following evacuation

Avoidance of Rectal Constipation —There is no possibility of having a

Courtesy of The E L P t h Company



A



B



C



D



E



F

Fig 440—Rectal diseases *A* Pruritus ani The skin around the anus is reddened and there are many characteristic folds *B* External hemorrhoids encircling prolapsed internal ones *C* Two internal hemorrhoids extending upward from the pectinate line *D* Vascular hemorrhoids *E* Hemorrhoid filling window of speculum *E* Hemorrhoid of type which lends itself very well to injection treatment *

Courtesy of The E L Patch Company

is prone are comforting in painful conditions such as thrombosed hemor rhoids ointments containing 1 or 2 per cent *nupercaine* or 3 to 10 per cent *ethyl aminobenzoate* give symptomatic relief in pruritus ani (p 1916) a vasoconstrictor spray of 1 1000 *epinephrine* may shrink a non thrombosed *hemorrhoid sufficiently so that it may be replaced*

The more ambitious local and topical remedies have greater commer cial and advertising value than palliative or curative potentialities *rectal dilators* devised mainly for the correction of fancied tightness of the sphincter have greater erotic than mechanical appeal medicated *supposi tories and ointments* advocated for the relief or cure of piles benefit the patient only if simultaneous replacement of the extruded mucou membrane is accomplished during the administration of the allegedly spe cific therapeutic agent The topical application of *sulfanilamide powder* or solution of *penicillin* (250 to 500 units to the cc) has potent anti infective power when there is an exposed surface

TREATMENT OF ANORECTAL CONDITIONS BY INJECTION AND SURGICAL PROCEDURES

Injection procedures are of value in the treatment of pruritus ani and hemorrhoids *alcohol injections* and *tattooing* allay intractable itching *sclerosing solutions* aid in the obliteration of the varicosity responsible for the hemorrhoid (p 1916)

Incision of a thrombosed hemorrhoid is simply accomplished The in cised area may be treated with powdered sulfanilamide or a packing that is saturated with penicillin containing 250 to 500 units to the cc Additional minor surgical procedures commonly practiced in routine work include cauterization *of an anal fissure with silver nitrate excision of* a *fissure* or fistula and hemorrhoidectomy (p 3947) The major procedure of abdomino perineal resection is discussed with the material on malignancy in this zone (p 1917)

CLINICAL DISTURBANCES

The clinical disturbances of the anorectal area include congenital ab normalities infections and inflammations mechanical disturbances vascu lar lesions and neoplasms

CONGENITAL ABNORMALITIES

IMPERFORATE ANUS

The imperforate anus is an uncommon congenital anomaly which is easily recognized Prompt surgical interference remedies the defect unless the infant has some more serious associated abnormality

PILONIDAL CYSTS

Pilonidal cysts are frequently observed some are dermoids and may contain hair and teeth Pilonidal cysts may not become apparent until adult life when attention is called to their presence as the result of sec ondary infection

Pilonidal dermoids and cysts are usually situated in the sacro coccygeal region They are recognized as localized swellings which are neither in flamed nor tender until secondary infection has occurred The occult vari

healthy anorectal region if the ampulla contains a wad of inspissated stool The fecal mass acts as a local irritant traumatizes the delicate mucous membrane and produces engorgement of rectal vessels favoring the production of hemorrhoids If the defecation reflex has been so blunted that the patient cannot be taught to have a daily morning evacuation the expulsion of the stool is accomplished by a simple rectal flush or the insertion of a glycerin suppository Ease of evacuation is favored by oral ingestion or rectal instillation of mineral oil (p 1825)

Curbing the Use of Drastic Cathartics and Saline Laxatives—Each physician knows from experience that violent purging may lead to traumatic proctitis erosion or ulceration of the membrane extrusion of rectal mucosa and an acute attack of 'piles In the majority of instances there existed little original indication for irritant catharsis in all likelihood the same benefits might have been derived at lesser cost through the use of a suppository a rectal flush or a simple soapsuds enema

Avoiding Excoriation from Toilet Paper—Modern civilization has probably devised few messier customs than that of the use of toilet paper Nowhere else in the body is it permissible to cleanse' by rubbing and spreading dirt from a localized to a wider area Aside from other considerations vigorous use of toilet paper produces local excoriation and erosion and may lead to many of the commoner pathological difficulties

It seems a pity that our engineering geniuses cannot devise some type of plumbing apparatus which like the bidet permits the user to flush the nether parts by means of a jet of water directed upward from the center of the bowl Until a plumbing revolution occurs the practitioner may teach his patient to improvise by directing a stream of water from a suspended enema bag to the region of the anal orifice Soft tissues rather than coarse toilet paper are then used to pat the area dry

Replacement of Rectal Mucosa—A prime cause of rectal difficulties particularly hemorrhoids is failure to replace extruded rectal mucous membranes after stool The everted membrane becomes edematous congested and irritated in the same manner as would the lip if the patient exposed that surface to atmospheric air for the greater part of the day It is inevitable that prolonged protrusion of rectal mucosa be followed by vascular thrombosis and production of the ugly and painful hemorrhoid

In our experience there is only one method of dealing with this situation Following evacuation the patient is ordered to apply soap and water to the perineal region After washing away the irritating soapy solution the index finger preferably protected by a rubber cot is lubricated and inserted into the anus in such fashion that the mucous membrane is completely replaced and held in position until there is the feeling that it will remain where it belongs Best results are accomplished if the operation is carried out during the course of a tub bath or shower

LOCAL AND TOPICAL REMEDIES IN THE TREATMENT OF ANORECTAL CONDITIONS

The simpler local and topical remedies are often efficacious in the symptomatic relief of anorectal disturbances the insertion of the *glycerine suppository* aids in the evacuation of the contents of the rectal ampulla *iced compresses* of water saline milk or witch hazel applied while the patient

is pore are comforting in painful conditions such as thrombosed hemorrhoids ointments containing 1 or 2 per cent *nupercaine* or 3 to 10 per cent *ethyl aminoben oate* give symptomatic relief in pruritus ani (p 1916) a vasoconstrictor spray of 1 1000 *epinephrine* may shrink a non thrombosed hemorrhoid sufficiently so that it may be replaced

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ety is often recognized by a dimpling of the skin or a hairy tuft overlying the tumor

Pilonidal cysts and fistulas require surgical treatment Dissection is often much more formidable than was originally suspected results are often unsatisfactory infection is inevitable from soiling due to the presence of feces and healing is poor Despite the seeming simplicity of the operation the practitioner is wise if he refers the excision of these tumors to the consulting surgeon

CONGENITAL RECTAL POLYPS

Congenital rectal polyps are frequently encountered when they become incarcerated and simulate hemorrhoids (p 1916) They are easily recognized by anoscopy and may be removed under local anesthesia using a snare

INFLAMMATIONS AND INFECTIONS

ANORECTAL MANIFESTATIONS OF THE VENEREAL DISEASES

The lesions of syphilis gonorrhea chancroid granuloma inguinale and lymphopathia venereum *may become manifest in the anorectal region* as the result of extension or from the practices of *sodomy* and *pederasty*

Primary syphilis (p 3278) appears as an indurated ulcer (chancre) at the anal margin or just within the anal canal the diagnosis requires *dark field microscopy* (p 45) *since the clinical features are by no means* sufficiently characteristic to warrant the institution of therapy without laboratory *confirmation*

The *secondary lesions of syphilis* particularly the mucous patches (p 3283) *appear in the region of the mucocutaneous junction of the rectum* These shallow ulcerations contain myriads of spirochetes and serologic tests are usually positive at this time Secondary syphilids have a tendency to appear as *condylomata lata* through maceration and admixture with *sweat and sebum The lesions are highly infectious and require* differentiation from *condylomata acuminata* (p 1914) which are nonspecific in origin Differential diagnosis requires *dark field examination* and *serologic tests*

The *soft chancre* of chancroidal disease may be anal in its location The *diagnosis is dependent upon positive identification of H ducreyi* together with negative darkfield microscopy The presence of *Donovan bodies* (p 2593) attests to the lesion of *granuloma inguinale* while *lymphopathia venereum* is proved by the *Frei test* (p 472)

The similarity in appearance of the various venereal infections requires that these conditions be suspected in any example of anorectal ulceration The practitioner recalls that multiple infections are possible he does not rest content until all of the evidence has been collected The required laboratory tests include *darkfield microscopy skin tests using Frei antigen* (p 473) and examination of *stained preparations* for *H ducreyi* (p 289) or *Donovan bodies* (p 475) *serologic tests for syphilis* are performed and the treatment schedule is guided by the positive findings

CRYPTITIS

The crypts situated at the anorectal junction are particularly vulnerable to irritative and inflammatory phenomena Fecal particles become inspissated producing erosion and infection

In most instances cryptitis produces no symptoms At most the patient notes *pain in the rectal region* a feeling of fullness or passages of *mucus* and/or streaks of *red blood* The examining finger palpates an area of *induration proctoscopy* reveals the presence of a local inflammatory process While the majority of infections of the crypts subside spontaneously others burrow subcutaneously to produce persistent *anal fissures* (p 1014) *perirectal abscesses* (p 1013) or *fistulas* (p 1014)

The *treatment* of cryptitis is most unsatisfactory Surgical interference is often ill advised The patient should secure as much palliation as pos

DIFFERENTIAL DIAGNOSIS OF

Ano perineal Pain

Pain in the perineum may be excruciating At times it is associated with spasm of anal or urinary sphincters producing tenesmus or strangury

	DIAGNOSTIC FEATURES
Anal	Fissures, fistulas papillitis cryptitis thrombosed hemorrhoids impaction of foreign bodies inspissated feces perianal abscess and ulcerated malignancy Obtain specimen for biopsy by anoscopy (p 1907) Proctitis from frequent and irritating stools following drastic cathartics or in association with regional ileitis colitis dysentery cholera and malignancies of the lower bowel Examine by sigmoidoscope and barium enema (p 1824)
Urinary	Strangury with calculous disease cystitis seminal vesiculitis prostatitis or ulcerating carcinoma of the prostate Following prostatectomy when indwelling catheter is left in situ Get urogram and consult urologist for cystoscopy (p 2242)
Gynecologic	In association with salpingitis, oophoritis pelvic peritonitis ulcerating uterine carcinoma and endometriosis Prepare for diagnostic dilatation and curettage (p 25[illegible]) Laparotomy if indicated

sible from *hot sitz baths* or *hot rectal irrigations* The canal is lubricated by oil taken orally or by rectal instillation

PAPILLITIS

The papillae in the region of the crypts (p 1012) frequently become inflamed and secondarily infected The condition is recognized by the proctoscopic appearance Local treatment is more satisfactory than is that of the cryptic infection

PERIRECTAL ABSCESS

Perirectal abscesses usually result from cryptitis They become manifest as *exquisitely tender swellings* in the *ischiorectal pelvirectal* or *retrorectal areas* After [illegible] they require wide excision and packing To [illegible] the cryptitis is treated during convalescence

FISTULA IN ANO

The fistula in ano is always a secondary phenomenon Most often it represents the external opening of a sinus tract that leads to a *cryptitis* (p 1912) a *tuberculous enteritis* (p 1860), a *regional ileitis* (p 1851) or a *chronic nonspecific ulcerative colitis* (p 1856) Following pregnancy many women develop *rectovaginal fistulas* as the result of birth trauma

The management of the rectal fistula is very difficult The tract will not heal as long as the more fundamental condition is operative Surgical dissection is required recurrences are frequent

PROCTITIS

Proctitis is often due to infections with the organisms that produce venereal disease With the increased prevalence of pederasty, *primary syphilis* and *condylomata lata* of secondary syphilis may be observed in this area the gonococcus may produce a cryptitis or a proctitis ulceration may be caused by the organisms of *lymphopathia venereum* (p 472), *granuloma inguinale* (p 475) or *chancroid* (p 289) These lesions can be identified by laboratory examination including *dark field microscopy* (p 45) and stains prepared for the identification of the gonococcus Ducrey bacillus and Donovan bodies (p 50) Proctitis also accompanies the perineal dermatoses such as scabies pediculosis pubis and fungous infections Treatment is accomplished by removal of the prime cause and measures of palliation (p 1910)

CONDYLOMA ACUMINATUM

Pointed condylomas (acuminata) result from nonvenereal infections of the anorectal regions They are differentiated from *flat condylomas* (lata) which are syphilitic in origin and highly infectious The definitive diagnosis requires darkfield microscopy (p 45) and serologic tests of the blood *Treatment* is palliative (p 1910)

MECHANICAL DISTURBANCES

Anal fissures and strictures prolapse and rectocele provide mechanical disturbances in the rectum Foreign bodies are occasionally impacted

ANAL FISSURES

In the majority of instances the anal fissure is produced by overzealous use of toilet paper or enema tips Superficial cracks heal readily when *touched* with silver nitrate or compound tincture of benzoin

RECTAL STRICTURES

Rectal strictures may be *congenital* in origin but most frequently are due to the late effects of *lymphopathia venereum* (p 472) The definitive diagnosis rests on the *Frei test* (p 473) Surprisingly favorable results are often associated with *sulfadiazine therapy* but in certain instances surgical intervention is required

Stenosis of the bowel may complicate endometriosis (p 2558) The rectal symptoms are associated with *menstrual irregularities and are relieved* by *castration* (p 2560)

PROLAPSE

Rectal prolapse may be *congenital* or *acquired* In the former instance conservative treatment is often successful The patient reclines during defecation and the buttocks are firmly strapped together after the bowel movement Surgical correction requires a formidable procedure which may not always be successful

RECTOCELE

The rectocele usually results from perineal laceration incidental to birth trauma The patient notes a dragging sensation in the rectal region and there may be difficulty in passing the stool The diagnosis is readily apparent particularly if examination is conducted while the patient strains

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DIFFERENTIAL DIAGNOSIS OF

Incontinence of Feces

Incontinence of feces may be psychogenic neurogenic or of local origin In any instance the condition requires a careful survey by anoscopy and barium enema

	DIAGNOSTIC FEATURES
Psychogenic	Carelessness and slovenliness Profound psychoses particularly general paresis and schizophrenia Get serology and spinal fluid examinations (p 3734)
Neurogenic	Cord tumors multiple sclerosis involving lower cord, transverse myelitis, hematomyelia syringomyelia and tabes dorsalis Perform motor and sensory examinations particularly of perineum (p 1490) Get blood and spinal fluid (p 3734)
Intestinal	Peristaltic rush, secondary to diarrheal conditions or violent purging
Anal	Tears of sphincter following labor or instrumentation. With hemorrhoids fissures and fistulas
Poisonings	Acute alcoholism. Barbiturate poisoning

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while standing The *treatment* is *surgical* but operation should be deferred unless there are sufficiently disabling manifestations to warrant the procedure Even in the best hands the late results are not always wholly satisfactory

FOREIGN BODIES

Children mentally disturbed patients and sex perverts occasionally insert foreign bodies in the rectum which cannot be removed Not infrequently enema tips break off or dislodge in the anal canal and thermometers occasionally slip up into the lumen of the gut

Removal is best effected under direct vision using an operating proctoscope

Vascular Disturbances

Hemorrhoids

Vascular disturbances of the anorectal region produce hemorrhoids one of the most commonly encountered conditions in routine clinical practice The disturbance is almost universal in pregnant women the constipated and those whose occupation requires prolonged standing The hemorrhoids may be external or internal uncomplicated thrombosed or ulcerated

External Hemorrhoid —External hemorrhoids appear acutely as firm tender and thick swellings which can be readily replaced within the anal ori-

DIFFERENTIAL DIAGNOSIS OF

Pruritus Ani

Itching of the anal region may be a maddening symptom that is exceedingly difficult to treat *In desperation, formidable measures must be employed for relief These include alcohol* injections radiation and tattooing

	DIAGNOSTIC FEATURES
Local Inflammatory	Impacted stool Uncleanliness Fissures and fistulas Prolapse of rectal mucosa Prolapsed external hemorrhoids Condylomas Pediculosis Dermatomycoses Diagnose by local inspection and anoscopy (p 1907)
Psychogenic	Frequent and intractable manifestation with secondary excoriations from scratching
Allergic	Particularly sensitivity to cascara phenolphthalein and opiates
Helminthic	Pinworms thread worms and uncinariasis Get specimen for ova and parasites (p 3731)
Metabolic	Jaundice cholemia gout or uremia with distinctive blood chemical findings Hyperthyroidism with elevation of B M R Diabete mellitus with glycosuria and hyperglycemia
Hematopoietic	Polycythemia vera Hodgkin s disease and leukemia Get hemogram or biopsy (p 3935)

fice if the attempt is made reasonably soon after the lesion has occurred (p 3947)

Thombosed External Hemorrhoid—After the hemorrhoid has been incarcerated for a variable period of time the vessel becomes thrombosed The patient suffers increased pain and the lesion appears bluish indurated and tense Often it cannot be replaced at all or if replaced it remains relatively unchanged

The thrombosed external hemorrhoid may terminate in one of four different ways Under most favorable circumstances the protrusion is replaced edema dissipates and healing occurs without leaving significant trace The next most favorable eventuality is healing with the production of a firm intravascular organized clot which invites later irritation and ulceration The irreducible external thrombosed hemorrhoid pursues a far less favorable course If pain is severe the physician may incise the skin

and evacuate the clot under which circumstance healing may be relatively uncomplicated as in the first two instances However if the protrusion is further neglected it ulcerates and produces the bleeding pile inviting local infection and increasing and recurrent difficulties

Treatment—The important principle of treatment of external hemorrhoids is prophylaxis (p 1910) Immediately the condition is encountered the pile is replaced if at all possible Local applications of cold wet dressings and a spray of 1 1000 epinephrine may permit the physician to replace the inflamed tissue The irreducible thrombosed external hemorrhoid requires *incision and evacuation (p 3947) Later it may be necessary to* perform a hemorrhoidectomy (p 3947)

Internal Hemorrhoids—Internal hemorrhoids differ from the external variety in that they are covered by mucous membrane rather than skin

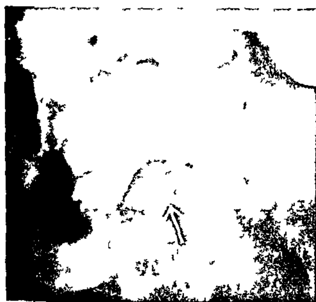


Fig 441—Carcinoma of the rectum Appearance produced by intraluminal protrusion of the tumor

Their position is easily recognized by palpation and anoscopy They are less accessible to the simpler methods of palliative treatment and often require *injection* therapy using sclerosing solutions (p *3946*) With persistent or accompanying external hemorrhoids operative procedure may be necessitated

NEOPLASMS

CARCINOMA OF THE RECTUM

Neoplasms in the rectum are usually malignant and occur at the rectosigmoid juncture in the ampulla of the rectum and within the anal canal The presenting symptoms are the appearance of *bright red blood* streaked

Buckstein Clinical Roentgenology of the Alimentary Tract

in the stool irregularities of bowel hygiene *pain* and *loss of weight* and *strength*

The *diagnosis* becomes apparent from digital exploration of the canal Sigmoidoscopy visualizes the lesion and enables the physician to obtain a specimen for biopsy

Surgical Treatment—With malignant lesions in the rectum it is necessary to establish a permanent colostomy Numerous operative procedures have been devised by single and multiple stage procedures The most common is *abdominoperineal resection* which is reserved for the treatment of carcinoma involving the distal portion of the sigmoid and the rectum In such cases the tumor cannot be sufficiently widely mobilized and resected through the abdominal approach In order to remove the lowermost segment of the bowel the abdominal operation is combined with an incision in the perineum Because of the fact that the rectum and anus are removed it is impossible to reestablish continuity of the bowel and preserve the anal sphincters The procedure therefore requires the establishment of a permanent colostomy in the abdomen

Abdominoperineal resection may be performed in one or two stages depending upon the general physical condition of the patient and certain technical considerations If performed in *one stage* the first portion of the procedure consists of an abdominal approach in which the tumor is mobilized from above as widely as possible The bowel is then clamped above the tumor and divided The upper loop is brought out upon the abdomen where it remains as a permanent colostomy The distal portion of the bowel bearing the tumor is then freed below the peritoneal reflection and pushed downward into the hollow of the pelvis The pelvic peritoneum is closed by suture

The patient is next turned on his side and an incision is made in the perineum in such a manner as to circumscribe the rectum The entire anus and rectum are freed upward into the hollow of the pelvis and the tumor bearing portion of the bowel which has been pushed below the peritoneal reflection is dissected out and removed through the perineal incision The entire perineal incision is packed with gauze

If the patient s general condition is not favorable or there are technical difficulties causing operation to be unduly prolonged the procedure may be performed in *two stages* The first stage establishes the permanent colostomy and the second stage consists of the actual removal of the tumor

The immediate risk varies between 10 and 20 per cent The posterior wound takes from two to six months to close completely There is a variable amount of postoperative urinary difficulty due to operative trauma to the nerves innervating the bladder The colostomy being low in the sigmoid functions well and if irrigated every twenty four to forty eight hours will not discharge except after irrigation thus obviating the necessity for wearing a colostomy pad

CHAPTER 95

THE PERITONEUM METHODS OF DIAGNOSIS AND TREATMENT CLINICAL DISTURBANCES

The peritoneum with an estimated surface area of 24 000 square inches is a vast membrane whose parietal layer lines the abdominal cavity The visceral layer constitutes the serosal covering of the intra abdominal organs and the two layers join to form the mesentery and the omentum

ANATOMY

The greater peritoneal cavity is directly entered upon incision of the abdominal wall It is arbitrarily subdivided into a central portion right and left lumbar gutters subphrenic (subdiaphragmatic) and subhepatic spaces and the pelvic peritoneum The central portion of the main peritoneal cavity is covered by the omentum the lumbar gutters are lateral to the ascending and descending portions of the colon the subphrenic spaces are situated posteriorly between diaphragm and liver while the subhepatic spaces are located anteriorly and are lateral to the falciform ligament The pelvic peritoneum is of greater significance in the female since the organs of reproduction have retained their embryological position in the abdominal cavity Pelvic peritonitis is a frequent accompaniment of adnexal disease and puerperal sepsis

The lesser peritoneal cavity is found posterior to the stomach It is entered through the foramen of Winslow just behind the pylorus

An appreciation of the extent of the peritoneal lining emphasizes the gravity of the diffuse inflammatory processes Knowledge of the anatomical subdivisions assists in the localization of abscesses preparatory to surgical incision and drainage

PHYSIOLOGY

In health the peritoneum functions to lubricate the outer surfaces of the intra abdominal organs A smooth glistening serosa is particularly required for the accomplishment of peristalsis in the serpentine loops of small intestine

In the presence of bacterial invasion the peritoneum has an inestimable defensive capacity The great omental surface is attracted to the site of the inoculum the outpouring of white cells in response to invasion produces a veritable leukocyte cream imprudent bacteria are phagocyted and digested with such speed and completeness that often there is no clinical manifestation of the hazard to which the host has been exposed For a single obvious example of infective peritonitis there must be hundreds of soilings of the cavity in which the invader has been liquidated The uneventful course that follows most intra abdominal operations attests to the powers of the peritoneum in withstanding bacteriological assaults

SPECIAL METHODS OF DIAGNOSIS

Aside from the information gleaned from the routine physical examination the practitioner includes in his diagnostic investigation abdominal puncture with the examination of the fluid that is obtained roentgen examination laparoscopy and exploratory laparotomy

Abdominal Puncture —Abdominal puncture (p 1823) provides absolute and indisputable evidence of a peritoneal exudate While it is perhaps not as safe a procedure as its most enthusiastic advocates aver it is far from being as dangerous and formidable as most practitioners and even surgeons insist

The puncture yields information which may save the patient an unnecessary and dangerous laparotomy and identifies the offending invader for chemotherapeutic purposes Fecal smelling exudate with a mixed gram negative and gram positive bacillary flora points to a perforating lesion of the hollow bowel which requires urgent intervention a pure culture of streptococci pneumococci or gonococci suggests a systemic infection in which operative intervention might be hazardous

Roentgenologic Examination —The demonstration of free air in the peritoneal cavity indicates perforation of a hollow viscus and calls for operative intervention as soon as the patient s condition warrants Roentgenograms are taken in the sitting and right and left lateral positions using the settings employed for the scout film (p 3741)

Laparoscopy (Peritoneoscopy) —Laparoscopy is an experimental procedure which utilizes the visual principles of bronchoscopy or cystoscopy for the investigation of the peritoneal cavity Since it requires a small incision into the abdominal wall in order to permit the entrance of the 'scope it would seem wiser to perform an exploratory laparotomy for direct and complete visual inspection and palpation

Exploratory Laparotomy —The practitioner reserves exploratory laparotomy as a last resort in his diagnostic investigation *It is safer to perform several unnecessary laparotomies rather than lose the opportunity to relieve a single example of acute appendicitis or intestinal perforation*

SPECIAL METHODS OF TREATMENT

Aside from systemic anti infective therapy of greatest utility in the acute peritoneal infections the treatment of peritoneal disorders may be accomplished by abdominal paracentesis and surgical intervention The latter may accomplish correction of a provocative lesion (reduction of hernia) excision of inflamed tissue (appendectomy) or the establishment of drainage

Abdominal Paracentesis —Abdominal paracentesis is performed with a trocar provided with a pointed obturator and an outlet arm to which is attached rubber tubing for the discharge of fluid

Before abdominal paracentesis the patient voids If there is any suspicion that the bladder is not empty catheterization is performed *Codeine or morphine* should be given fifteen minutes before the expected procedure The patient sits on the side of the bed each foot resting on a chair His back is supported by pillows or the back of an assistant seated on the other side of the bed The skin of the abdomen is shaved painted with tincture of iodine and washed with alcohol The patient is draped with sterile

towels leaving an area exposed in the mid line between the umbilicus and the symphysis pubis An abdominal binder with long ends and a hole in

DIFFERENTIAL DIAGNOSIS OF

Ascites

The peritoneal accumulation of large amounts of fluid gives rise to abdominal fullness In contrast to tympanites which is a gaseous distention, there is dulness in the flanks shifting of the note with change in position, and elicitation of a fluid wave

	DIAGNOSTIC FEATURES
Toxic or Metabolic	
Hypoproteinemia	Particularly in the nephrotic syndrome with massive albuminuria and hypercholesterinemia Also observed in eclampsia with hypertensive toxemia of pregnancy albuminuria and convulsions
Infectious and Inflammatory	
Peritonitis	Particularly tuberculous pneumonic and non specific types Obtain fluid by diagnostic puncture and stain and culture for identification of pathogen (p 50) Inject into guinea pig on suspicion of tuberculosis (p 62)
Polyserositis	With pericarditis and pleural effusion
Filariasis	Found worm infection with lymph stasis and fibrosis leading to chylous ascites Microfilaria in blood film obtained at night
Neoplastic	
Benign Tumors	With ovarian cysts and large uterine fibroids Confirm pelvic examination by laparotomy (p 1920)
Malignant Tumors	With metastatic carcinomatosis and primary intraperitoneal malignancies of stomach ovaries and uterus Look for tumor cells in fluid obtained by diagnostic aspiration (p 1823)
Hepatic	
Atrophic Cirrhosis	Particularly in alcoholics with progressive diminution in the size of the liver frequent hematemesis and late appearance of jaundice
Biliary Cirrhosis	In younger individuals with enlargement of liver fever leukocytosis abdominal pain and early and marked jaundice
Circulatory	
Backward Failure	With dyspnea cyanosis edema and pulmonary hypostasis May be relieved by mercurial diuretics
Venous Obstruction	Particularly of portal vein inferior vena cava and mesenteric vessels

the center is placed around the abdomen of the patient so that intra abdominal pressure may be maintained during the removal of the fluid

The skin is anesthetized with 2 per cent procaine for a distance of 1 inch just lateral to the mid line about half way between the umbilicus and symphysis The subcutaneous tissues down to and through the linea

alba, are infiltrated With a sterile scalpel the skin is incised to a depth of about ½ inch The incision is carried through the subcutaneous tissue to the linea alba until there is sufficient opening for the introduction of the trocar and cannula Rubber tubing about a foot long is attached to the opening at the side of the cannula

The trocar and cannula are gently pushed through the opening of the skin through the fascia and into the peritoneal cavity At this point the trocar is withdrawn, leaving the cannula in place The fluid is collected in an ordinary bucket or in a sterile flask

If the flow ceases while there are still physical signs of free fluid the cannula may be manipulated and the trocar reintroduced in a very gentle fashion If there is still no flow the patient is instructed to lean forward placing his hands on the shoulders of the operator who is seated on a stool before him Fluid from the lumbar gutter gravitates centrally The cannula is slowly withdrawn so that the last remains of the fluid are drained Dry dressings are placed over the puncture wound a tight binder is applied and the patient is then permitted to recline in bed

If the patient becomes faint during the course of the paracentesis aromatic spirits of ammonia will usually be sufficiently effectual Drainage may persist through the puncture wound for a considerable time

The chief *complications* of abdominal paracentesis are perforation of a hollow viscus and injury to the deep epigastric artery The former is largely prevented by having the bladder empty before starting the procedure and inserting the trocar in an area of definite dulness The latter may be avoided by staying as close as possible to the midline

Patients who cannot sit up for the paracentesis may be tapped laterally at a point corresponding to the edge of the rectus sheath This site is approximated by the junction of the outer and middle thirds of a line joining the anterior superior spine of ilium and the umbilicus

CLINICAL DISTURBANCES

The peritoneum may be the site of disturbances which result from congenital abnormalities inflammations and neoplasms Mechanical and vascular disturbances are rarely encountered

Congenital Abnormalities
- Mesenteric and Omental Cysts
- Peritoneal Bands and Veils (Jackson's Membrane)

Inflammations
- *Peritonitis*
  - Fibrinous Peritonitis
  - Exudative Peritonitis
  - Gangrenous Peritonitis
  - Localized Suppuration
    - *Appendicular Suppuration*
    - Pelvic Suppuration
    - Pericolonic Suppuration
    - Subphrenic Suppuration
    - Perihepatic Suppuration
  - Chronic Peritonitis
  - Hematogenous Peritonitis
  - Lymphogenous Peritonitis
  - *Pneumococcal* Peritonitis
  - Gonococcal Peritonitis
  - Tuberculous Peritonitis
    - Acute Tuberculous Peritonitis
    - Chronic Tuberculous Peritonitis
  - Aseptic Peritonitis
  - Peritonitis from Penetrating Wounds
  - Peritonitis in the Newborn
  - Postoperative Peritonitis
  - Adhesive Peritonitis
  - Proliferative Peritonitis

Neoplasms
- Primary Neoplasms
- Secondary Neoplasms

Miscellaneous
- *Torsion of Omentum*
- Fat Necroses
- Mesenteric Thrombosis

MESENTERIC AND OMENTAL CYSTS

Mesenteric and omental cysts occur as rare congenital lesions The tumors are usually single and about the size of a plum but they may be very much larger their content consists of a watery or milky fluid

Mesenteric and omental cysts become clinically manifest in childhood or early youth when attention is directed to a movable mass which may rapidly increase in size The patient remains free from symptoms and enjoys a state of well being

Exploratory laparotomy reveals the nature of the disturbance and therapy consists of excision

PERITONEAL BANDS AND VEILS (JACKSON S MEMBRANE)

Congenital bands and veils are frequently observed as chance findings in the exploration of the peritoneal cavity They are of no importance unless they produce *intestinal stenosis* or *obstruction* (p 1873) Under these circumstances division of the band may be the only surgical procedure required provided the involved loop of gut is viable

PERITONITIS

Inflammation of the peritoneum presents a variety of complicated problems The clinical manifestations and the indications for treatment are modified by many variables which include the nature of the pathologic process the pathogenesis of the disease the type of bacterial invader and the presence or absence of associated disturbances Peritonitis is not to be regarded as a single clinical entity whose management can be routinized Each patient afflicted with this serious inflammatory process presents a unique problem whose elucidation requires thoughtful consideration on the part of the practitioner and his surgical consultant

Pathology —The earliest inflammatory change in a peritonitis is the laying down of fibrin The normally transparent and glistening surface becomes dull opaque and injected The fibrinous exudate glues together the coils of intestine and a yellow serofibrinous fluid accumulates in the free peritoneal cavity With advance in the inflammatory process the exudate becomes purulent

In unfavorable instances the peritoneal reaction spreads the patient becomes highly septic and may succumb unless the course can be halted by treatment In the most favorable instances the inflammatory process subsides with complete restitution to normal Between the two extremes there may be healing by scar formation or localization with suppuration In the former instance the patient is left with a *chronic adhesive peritonitis* In the latter circumstance the course is ordinarily interrupted by surgical incision with drainage of the abscess

Pathogenesis —Peritonitis may be of local or remote origin *Intra-abdominal causes* are (1) *direct extension* of infection (appendicitis leakage from an appendiceal stump or an intestinal anastomosis) and (2) *introduction of fecal bacteria* as a result of perforation of an ulcer or a neoplasm Peritonitis also arises as the result of dissemination of infection from a distant source by *hematogenous* or *lymphogenous routes* Thus the upper respiratory infection may be associated with a peritonitis in which the organism is carried by way of the lymphatics Patients weakened by chronic disease develop a terminal hematogenous peritonitis as illustrated by the pneumococcal invasion that concludes the history of the nephrotic stages of kidney disease

The practical importance of the recognition of the pathogenesis of peritonitis rests in the surgical implications In those *infections of local origin* the operative desideratum is early interference at a time when the inflammation is still localized and its cause can be readily and rapidly eliminated Laparotomy during the later spreading diffuse stage accomplishes

little at tremendous risk and it is not until localized suppuration has occurred that the abdomen can again be entered with safety and a promise of the amelioration of conditions By contrast *hematogenous and lymphogenous invasions* begin as diffuse processes early operative interference is ill advised and optimal management focuses upon anti infective therapy and serotherapy The abdomen is not entered until the acute episode has significantly abated when incision is required for drainage of a localized abscess

Bacteriology—The peritoneal infections of local origin usually yield a variety of organisms by both smear and culture *Streptococci coliform bacilli* and *gram positive anaerobes* of the gas gangrene variety are usually demonstrable streptococci produce a thin serosanguineous fluid that is highly toxic anaerobic infection gives a greenish gangrenous pus with a foul odor

Hematogenous and lymphogenous forms of peritonitis are most often due to the coccal organisms *beta hemolytic streptococci pneumococci* and *gonococci* invade the intra abdominal cavity which may also be attacked by the *tubercle bacillus*

FIBRINOUS PERITONITIS

The practitioner attempts to recognize peritonitis in the early fibrinous stage and to determine whether the involvement is localized as in peri appendicitis or diffuse as in a pneumococcal invasion With a fibrinous peritonitis the patient complains of *pain* that is usually referred to the site of the lesion This is well illustrated in appendiceal infections The practitioner recalls that the earliest localization of pain in acute appendicitis is epigastric or peri umbilical This misleading reference of pain is due to visceral involvement and it is not until the peritoneum becomes inflamed that the complaint shifts to the right lower quadrant

Clinical Manifestations—Peritoneal pain is usually intense and accompanied by *rising temperature leukocytosis* evidences of *shock* and *collapse chilliness* or an actual *chill nausea vomiting* progressive *constipation* and *hiccough* The extent of the constitutional manifestations is dependent for the most part upon the reactivity of the patient Overwhelming infection in debilitated patients produces insignificant evidences of fever leukocytosis shock collapse or chilling

The *vomiting* of peritonitis increases abdominal discomfort at first the vomitus consists of stomach contents later bile stained duodenal fluid is expelled and finally in the neglected types of peritonitis with paralytic ileus the emesis is fecal in appearance and odor

At the onset of a peritonitis there may be some *hyperperistalsis* as manifested by one or several loose small evacuations Eventually however an *obstinate constipation* is experienced with loss of peristalsis atony and dilatation of the bowel The appearance of *hiccough* has ominous significance and usually means irritation of the diaphragmatic surface (p 1933)

In the fibrinous stage of peritonitis the patient reveals very characteristic physical findings He usually lies on his back with thighs drawn up and shoulders hunched as if attempting to protect and narrow the peritoneal cavity, respirations are shallow and costal in type due to reflex splinting of the diaphragm any movement or pressure aggravates discomfort and the sufferer appears tense and anxious

Local examination discloses marked *tenderness* which may be diffuse or localized and the more revealing sign of *involuntary rigidity* (p 1746) The latter most important to elicit (p 3508) is the earliest and most significant indication of the nature of the pathological process It is sought

with exquisite gentleness Whether or not corroborative evidences are present it cannot be denied It demands *surgical consultation* (p 3655) and further investigation by *abdominal puncture* (p 1893) or *laparotomy* (p 1930)

Involuntary rigidity of the abdominal wall is usually accompanied by *direct* and *rebound tenderness* The former is of greatest significance when it is sharply localized as over the right lower quadrant in appendicitis Rebound tenderness (which is noted when the examining hand is suddenly withdrawn from the abdominal wall) usually but not invariably indicates peritoneal irritation It is a highly suggestive finding but has not the absolute value of involuntary rigidity

The results of abdominal palpation are often confirmed by examination of the pelvic diaphragm through *rectal* and/or *vaginal exploration* Localized tenderness and rigidity are corroborated by abdomino-rectal or abdomino-vaginal methods Occasionally retroperitoneal infections as in an appendicitis are more clearly delineated by internal examination alone

Diagnosis.—The routine blood count and estimation of the sedimentation rate (p 3707) give valuable information in peritoneal inflammation Assistance is also obtained from abdominal puncture roentgenography (p 3740) and exploratory laparotomy Peritoneoscopy has not yet attained the position of a routine procedure of acknowledged merit

Complications.—The principal complications of *acute peritonitis* are paralytic ileus and sepsis each of which predisposes to the development of the other With paralytic obstruction of the bowel the intestines dilate and favor the passage of bacteria into the blood stream the toxemia of sepsis favors paralytic distention of the bowel

Chronic peritoneal infections are often silent unless intestinal obstruction is produced

Course.—The course of a peritonitis may be acute subacute or chronic Fulminating episodes usually eventuate in a quick decision of death or complete recovery subacute and chronic types of inflammation are more likely to end with adhesive peritonitis or localization and abscess formation

Intraperitoneal abscesses are most often evacuated by the surgeon Untreated they tend to abort spontaneously rupture into the lumen of a hollow viscus with satisfactory drainage or break into a near organ with further propagation of the infection

Treatment.—The treatment of peritonitis cannot be routinized Individual problems require the close cooperation of surgeon and practitioner Patients require ante-operative and postoperative medical care If immediate surgery cannot safely be accomplished the surgeon must stand by and be prepared to share the responsibility of conservative treatment and when the time seems opportune proceed with operative intervention

Nonoperative Treatment.—The supportive program in the conservative treatment of diffuse peritonitis requires that food and fluid be forbidden by the oral route The patient is given an *intravenous drip* of 5 per cent dextrose solution in saline to the amount of 2500 to 3000 cc daily In addition *transfusions* are administered at regular intervals Peristalsis is inhibited by small doses of *opium* when required The peristaltic stimulants such as cathartics neostigmine and pitressin are contraindi

cated The removal of toxic intestinal content is accomplished by *intubation* and *continuous suction drainage* using the Wangensteen apparatus attached to the Miller Abbot tube (p 1823)

Combined antibiotic therapy is instituted using parenteral injections of streptomycin (p 104) and penicillin (p 106) These may be supplemented by oral streptomycin and/or sulfadiazine (p 88) if the situation is critical or the progress of events is unsatisfactory

Operative Treatment—Operative intervention in acute peritonitis requires the most mature judgment relative to the time of procedure and the technic to be followed In the *lymphogenous and hematogenous varieties* operation is deferred until there is sharp localization and abscess formation with frank pus In the forms of peritonitis that occur by *local extension* there is general agreement that early operation is imperative but in the stage of diffuse peritonitis the risk of laparotomy is greatly increased Peritonitis due to rupture of a hollow viscus demands immediate surgical intervention despite the presence of infection and shock The operative mortality rises in direct relationship to the span of time that transpires between the accident and the surgical effort

In the chronic forms of peritonitis aside from the drainage of localized abscesses operative intervention is fraught with great danger The anatomical landmarks are obscured by the matted adhesions and there is the ever present danger of inadvertently producing a penetration or perforation of a loop of bowel

EXUDATIVE PERITONITIS

With outpouring of a significant quantity of free fluid into the peritoneal cavity the patient often exhibits relief from the discomfort of the fibrinous peritoneal response Ascites develops particularly in pneumococcal (p 1929) and tubercular (p 1930) infections With large quantities of fluid, considerable mechanical distress is produced within abdominal and thoracic cavities

Abdominal paracentesis (p 1920) has both diagnostic and therapeutic usefulness After the tap masses may be palpated though they were not previously felt the fluid is examined by spread culture and guinea pig inoculation in order to clarify etiology and indications for therapy

GANGRENOUS PERITONITIS

In the presence of overwhelming peritoneal infection and in patients who are debilitated by chronic disease the deceptive soft belly peritonitis is encountered This condition may or may not be preceded by the manifestations of a fibrinous reaction (p 1924) The transition from fibrinous to gangrenous peritonitis is marked by amelioration of pain tenderness and involuntary rigidity The apparent relief is associated with increased toxemia and tachycardia

In patients with chronic illness or debilitating disease gangrenous peritonitis develops insidiously and is often revealed only at autopsy There is rarely any subjective recognition of the infection The classical physical findings of peritonitis are notably absent though careful and repeated examination may disclose some slight tenderness some increase in disten

tion and greater difficulty in producing a satisfactory bowel evacuation At times the first intimation is the demonstration of free fluid in the abdomen (p 1921) Abdominal puncture yields purulent material rather than the expected ascitic fluid

Gangrenous peritonitis is invariably associated with *sepsis* and *toxic ileus* the diaphragm is pushed high into the thoracic cavity the apex heart beat is dislocated liver dulness is reduced and even completely obliterated auscultation of the abdomen yields the ominous silence of a tomb the high diaphragm with its underlying distended and tympanitic gut produces all manner of deceptive pulmonary signs over the lower lobes of both lungs the sensorium becomes progressively clouded and the patient may be comatose or delirious Characteristically there is the gruesome picking at the bedclothes and the patient finally succumbs the body appearing like a hideous caricature of its pristine self The overall picture fulfils the classical description of the Hippocratic facies— the sharp nose hollow eyes and collapsed temple the ears cold contracted and their lobes turned out the skin about the forehead rough distended and parched the color of the whole face brown black livid or lead colored

Treatment —The tragedy of the Hippocratic picture of peritonitis lies in the fact that the syndrome is preventable in the vast majority of instances It is the responsibility of the patient and practitioner to cooperate in the prevention of diffuse and generalized acute peritonitis The patient does his share by reporting to the physician early and minimal symptoms of abdominal distress The practitioner s function is to render an early diagnosis and institute a vigorous therapeutic regimen at the beginning of peritoneal infection This he does by the combination of anti infective therapy and surgery

Even with the ominous picture of a gangrenous peritonitis the practitioner does not abandon his efforts at saving the life of the patient A continuous intravenous drip is established to this saline dextrose plasma and whole blood are added antibiotic therapy is conducted with large doses of streptomycin (p 104) and penicillin (p 106) and sufficient sulfadiazine (p 88) is given in the drip or orally in order to maintain a level of at least 8 mg per cent Zealous nursing care may prevent many of the dire complications such as bedsores hypostatic pneumonitis and parotitis Morale is upheld by sustained effort rather than forced optimism Occasionally all are rewarded by the collection of laudable pus which may be evacuated by simple surgical incision

SUPPURATIVE LOCALIZED PERITONITIS

When acute peritonitis has subsided localizations often occur in favored localities Those most frequently encountered include appendicular pelvic pericolonic subphrenic and subhepatic collections

Appendicular Abscesses —Acute appendicitis frequently terminates in a peri appendicular abscess This condition rarely offers diagnostic difficulty since there is usually an antecedent history which suggests the acute inflammatory process With the subsidence of systemic manifestations the tumor mass is noted in or about the right lower quadrant Occasionally it is best felt by rectal or vaginal examination The abscess requires incision and drainage Antibiotic therapy is begun or continued

Pelvic Abscesses—Pelvic peritonitis is most often of *gonorrheal origin* (p 1930) With subsidence of the acute inflammatory signs, an exudate is easily delineated by rectovaginal palpation Occasionally, pelvic abscesses result from appendiceal inflammations diverticulitis or the penetration of a colonic neoplasm (p 1889)

Pelvic abscesses of gonorrheal origin may subside after intensive anti infective therapy If they persist incision and drainage are required

Pericolonic Abscess—*Right-sided* pericolonic abscesses are usually due to appendicitis and often terminate in subphrenic collections next to be described *Left sided* pericolonic abscesses produce the highly characteristic symptoms of a sudden inexplicable *diarrhea* experienced during the course of recovery from some intra abdominal operation Occasionally the abscess ruptures into the lumen of the bowel and successfully becomes evacuated without the need for operative interference

Persistent pericolonic abscess refractory to anti infective therapy must be incised and drained

Subphrenic (Subdiaphragmatic) Abscess—The subphrenic abscess often gives rise to considerable diagnostic difficulty Its commonest cause is *acute appendicitis* with *peritonitis* or *pylephlebitis* (p 1961) The patient having progressed relatively uneventfully for a time develops severe upper abdominal pain tenderness and vomiting respirations are embarrassed due to diaphragmatic spasm constitutional symptoms arise and chills occur with a septic type of temperature The patient pursues a progressively downhill course unless the abscess can be localized and drained surgically The most consistent finding is *jar tenderness* over the costal arch there may be some *jaundice* in a small percentage of these patients perforation occurs through the diaphragm and into the free pleura or the lungs resulting in the production of an *empyema* or a *lung abscess*

Upon suspicion of the development of a subphrenic abscess a surgical consultant is summoned In the operating room under anesthesia the subphrenic space is approached with an aspirating needle as soon as pus is obtained the needle is left in situ and drainage is instituted by rib resection and posterior approach

Perihepatic Abscess—Perihepatic abscess appears beneath the arch of the diaphragm to the right or left of the falciform ligament The diaphragm is pushed high into the thorax and respiratory symptoms may predominate to the point that an empyema is suspected All manner of atypical pulmonary signs are manifest due to compression of the lungs the height of the diaphragm and the physical conditions of the inflammatory perihepatic tissue

Without accurate interpretation of a radiograph the diagnosis of a perihepatic abscess is quite impossible When the lesion is caused by gas producing organisms the fluid pus and air within the abscess cavity give the physical signs of a pyopneumothorax (p 2219)

The perihepatic abscess should be drained by abdominal incision as soon as the localization has been completed

HEMATOGENOUS STREPTOCOCCAL PERITONITIS

Hematogenous streptococcal peritonitis occurs most often as an agonal and insidious manifestation in chronic debilitating disease The patient

complains of some abdominal distress the physician observes distention increased constipation vague tenderness and the development of a small amount of free fluid in the peritoneal cavity The symptoms are masked by the clouding of consciousness and the patient s inability to react Rarely is there any significant elevation of temperature or leukocyte count

Even with intensive supportive and anti infective therapy the patient usually proceeds unfavorably and dies At autopsy there is the surprising and often unforeseen finding of a diffuse streptococcic peritonitis with serous exudate but little fibrin

LYMPHOGENOUS STREPTOCOCCAL PERITONITIS

Lymphogenous streptococcal peritonitis occurs most often in childhood as the result of an upper respiratory infection particularly *tonsillitis* (p 2154) The usual history is that of *abdominal pain* and *tenderness* in a child who is afflicted with or convalescing from a tonsillar infection Examination reveals evidence of peritoneal irritation accompanied by a rise in temperature and a leukocytosis The natural suspicion is a coincidental *acute appendicitis* (p 1881) The diffuse signs are interpreted as the result of a spreading peritonitis due to gangrene of the appendix or actual perforation

At operation the appendix is found to be normal, but the peritoneal surfaces are dull, congested and covered with fibrinous exudate There may be an associated swelling and engorgement of the mesenteric lymph nodes (*tabes mesenterica*) Often there is a small amount of free fluid of a sero sanguineous nature

Despite the temptation to leave the appendix rather than open new channels for infection an *appendectomy* is usually performed Intensive antibiotic treatment with penicillin (p 106) and streptomycin (p 104) is begun

PNEUMOCOCCAL PERITONITIS

Pneumococcal peritonitis occurs as a primary condition in young girls as a terminal invasion in nephrosis (p 2389) and as a complication of lobar pneumonia (p 2171)

Primary Infection in Young Girls.—Primary pneumococcal peritonitis in young girls is a virulent infection with acute onset and overwhelming systemic signs The disease usually occurs in patients between the ages of three and seven at a time when the vaginal secretion is alkaline The rarity of this disturbance in boys suggests that organisms are aspirated through the fallopian tubes The more frequent occurrence of the disease in poor children indicates that insufficient clothing and inadequate perineal protection may be factors in the pathogenesis of the disease

The diagnosis of pneumococcic peritonitis is suspected when the child gives evidence of peritoneal irritation The condition is proved by the demonstration of the organism in peritoneal exudate obtained by *abdominal puncture* or *laparotomy*

The condition is treated by *intensive anti infective therapy* supplemented by *specific serotherapy* if a typed pneumococcus is obtained. The virulence and high mortality of the affliction demand the use of every possible therapeutic modality in vigorous and full dosage.

Terminal Infection in Nephrosis.—Pneumococcic peritonitis occurs as a

terminal complication in nephrosis (p 2389) The child, previously afebrile develops pyrexia and characteristic peritoneal signs Abdominal puncture reveals the organism Specific anti infective therapy with penicillin (p 106) is advisable since the course of the disease is usually progressively unfavorable terminating in death

Para or Post pneumonic Peritonitis —Pneumococcal peritonitis may ac*company or follow pneumonitis The complication* may be hematogenous or it may travel by way of the lymphatics from a suppurative process above the diaphragm (pneumococcic pleurisy or empyema)

The diagnosis of pneumococcal peritonitis is often difficult since the toxic manifestations of pneumococcemia include paralytic ileus with resultant abdominal distention and discomfort The progression from toxic *ileus to inflammatory peritonitis may be imperceptible, in consequence of* which the condition is often an unsuspected autopsy finding

The astute practitioner will suspect a pneumococcal peritonitis if abdominal pain is severe and persistent, if distention is not controlled by the ordinary measures (p 2177) or if there is associated involuntary muscle rigidity of the abdominal wall and progressive toxemia Abdominal *puncture disclosing the organism establishes the diagnosis with assur*ance The pneumococcus is typed and specific serum is added to the anti infective remedies An exploratory laparotomy at this time is dangerous and may be an agonal effort

GONOCOCCAL PERITONITIS

Gonococcal peritonitis usually occurs as an extension of *tubo ovarian infection* (p 2608) In rare instances it is hematogenous and may occur in the male as well as in the female

The symptoms consist of agonizing *pain* with *pyrexia* and *leukocytosis* in an individual known to have been infected with the gonococcus Ordinarily the inflammatory exudate is fairly well localized to the pelvic peritoneum *It tends to chronicity with the formation of dense fibrous ad*hesions

The *diagnosis* is suspected through the coexistence of a gonorrheal infection in the urethra or adnexa and the manifestations of peritoneal irritation With right sided symptoms it is impossible to be certain that there is not present an associated or independent acute appendicitis *The practitioner recalls* that the patient with gonorrheal urethritis may as well as any one else develop an acute inflammation of his vermiform appendix If there is any doubt it is wise to perform an exploratory abdominal puncture If a gram negative diplococcus is clearly demonstrable anti infective therapy is indicated as exploratory laparotomy is hazardous with little promise of amelioration of symptoms By contrast the recovery of a gram positive streptococcus or bacillary forms suggests the possibility of an appendiceal inflammation and warrants surgical exploration

TUBERCULOUS PERITONITIS

Tuberculous peritonitis may be acute or chronic localized or diffuse plastic or effusive It may occur without other demonstrable intra abdominal *lesions* under which circumstance it is hematogenous or lymphog

enous but it may also accompany tuberculous enteritis lymphadenitis or salpingitis

Acute Tuberculous Peritonitis—Acute tuberculous peritonitis is seen most frequently in infancy and early childhood With or without a pre existent tuberculous process the patient develops an extensive intra ab dominal effusion Abdominal puncture reveals a clear fluid containing lymphocytes On injection the specimen produces tubercular lesions in guinea pigs

Acute tuberculous peritonitis may also develop as an extension in a patient who has intestinal glandular or adnexal involvement Under these circumstances the symptoms of peritoneal irritation are superimposed upon those of the preexisting lesion Intensive therapy with streptomycin (p 104) warrants trial

Chronic Tuberculous Peritonitis—Chronic tuberculous peritonitis may be come manifest as an *ascites* with lymphocytic fluid or it may produce a diffuse *plastic and adhesive inflammation*

In the *moist types* of chronic tuberculous peritonitis the picture is that of great abdominal distention occurring in a cachectic patient The aspirated fluid is usually clear but may be hemorrhagic It is rarely pos sible to demonstrate the causative organism by smears and cultures but injection into the guinea pig reveals characteristic lesions

If operation is performed miliary tubercles may be demonstrable on the peritoneal surfaces large caseating lymph nodes may also be observed intestinal fistulas may be present as well as loculated pools of fluid con tained in dense adhesions

In the *dry forms* of chronic tuberculous peritonitis a dense plastic exudate all but obliterates the free peritoneal cavity and mats the intes tine in bizarre patterns Despite the extensive nature of the pathological process there are relatively few symptoms or signs unless an intestinal obstruction is produced The abdominal wall may be board like (*ligne ous*) without any apparent clinical discomfort or embarrassment

The *treatment* of the exudative type of chronic tuberculous peritonitis is by an exploratory laparotomy For some reason that is not at all clear many patients seem to improve as the result of the mere opening of the abdominal cavity If an easily removable focus is in clear view (caseat ing lymph nodes or adnexal disease) excision may prove to be salutary In the plastic types of inflammation surgical intervention holds promise of nothing but more trouble The division of adhesions is soon followed by their re-formation meddlesome tinkering may lead to obstruction or per foration Intensive therapy with streptomycin (p 104) warrants trial

ACUTE PERITONITIS COMPLICATING INTRA ABDOMINAL DISEASE

Acute peritonitis may arise as a localized or diffuse inflammation result ing from the *direct extension* of an infectious process that involves the wall of an intra abdominal organ or it may be caused by *penetration or perforation* in which bacteria are introduced into the free peritoneal cavity In a relatively few instances the peritoneal reaction results from an *aseptic cause* The preponderant majority however are *bacterial* in origin

Aseptic Peritonitis—The presence of irritating sterile material occasion ally gives rise to an intense peritoneal reaction The more frequent causes

are the extravasation of *bile* from the rupture of a hydrops of the gall bladder the presence of *blood* derived from an *ectopic pregnancy* or a ruptured *ovarian cyst*

In these circumstances the patient suffers severe *pain* which may be sufficient to produce *collapse* There is a disproportionately small amount of muscle tenderness and rigidity in relation to the subjective anguish Despite the aseptic character of the exudate there may be elevation of temperature and leukocytosis

Abdominal puncture reveals the nature of the extravasated fluid The presence of *bile* leaves no doubt as to the diagnosis and indicated operative procedure If bloody fluid is obtained and there is a history of a skipped menstrual period an *ectopic pregnancy* (p 2657) is suspected If an attack occurs between the ninth and twelfth days following the initiation of a previous menstrual period there is a strong suggestion that the bleeding is a manifestation of *dysovulation* (Mittelschmerz) (p 2528)

Peritonitis from Penetrating Wounds —Infection may be introduced into the peritoneal cavity by penetrating wounds of the abdominal wall or the perforation of a uterus by a curette usually in the course of an illegal abortion

The indication is for immediate laparotomy with preoperative and post operative fortification by anti infective agents plasma and blood

Peritonitis in the Newborn —*Peritonitis occurs in the newborn as the* result of an extension of infection from an inflamed *cord* The streptococcus is the usual invader

The *infant shows* distention of the abdomen with redness and swelling of the umbilicus Not infrequently *jaundice* is present A significant febrile reaction may be lacking due to the overwhelming nature of the infection and feeble resistance of the child

The *treatment* is chemotherapeutic operative interference is avoided

Postoperative Peritonitis —Postoperative peritonitis often follows technical errors such as contamination the leakage of the suture lines in the various types of anastomosis and unavoidable soiling through the appendiceal stump

The initial symptoms are usually *abdominal distress* and *pain* There is increasing and intractable *distention* elevation of temperature and leukocytosis

Many surgeons are reluctant to admit that peritoneal inflammation has occurred and seek to incriminate a lesion above the diaphragm such as a pneumonitis or a pyelitis If the practitioner is sure that there is inappreciable pulmonary involvement and the urine specimens are clear he should insist upon the consideration of a peritoneal complication

A surgical revision is often necessitated and the patient is sustained by local and systemic chemotherapy using streptomycin (p 104) penicillin and/or sulfonamide

CHRONIC PERITONITIS

Chronic peritonitis may be a sequel of the acute type or it may be an indolent infection from the beginning as in tuberculosis The extent of a chronic peritonitis varies between localized abscess formation as in appendicular peritonitis to a diffuse and generalized form as seen in tuberculosis

The nature of the peritoneal reaction is subject to modification There

may be *fibrous adhesions* which give evidences of clinical disturbance only through obstruction of the hollow viscera There may be an *effusion* which cannot be differentiated from noninfective forms of ascites (p 1921) There may be localized collections of *pus* occurring in various sites of election such as the right lower quadrant in appendicitis the subphrenic space or the pelvic peritoneum

The bacteriology of chronic peritonitis often remains obscure since purulent processes undergo a process of autosterilization Tuberculosis is always

DIFFERENTIAL DIAGNOSIS OF

Hiccough (Singultus)

Hiccough is produced by convulsive contractions of the diaphragm The disturbance may be purely functional in origin or it may be organic due to a neurogenic or diaphragmatic lesion

	DIAGNOSTIC FEATURES
Psychogenic	In hysteria
Neurogenic	With encephalitis and encephalopathies Supplement neurologic examination with examination of cerebrospinal fluid (p 3734) From vagal irritation due to mediastinal inflammation, caseation of mediastinal lymphnodes adherent pericardium or hypertrophy of left auricle Supplement physical examination with x rays of chest (p 3740) In crises of tabes dorsalis with characteristic pupillary and reflex *changes and abnormalities of cerebrospinal* fluid (p 1464)
Toxic and Metabolic	In acute and chronic alcoholism With azotemia and impairment of renal function
Digestive	From overdistention of stomach, air swallowing bolting of food and ingestion of irritant spices or carbonated drinks particularly of high alcoholic content. With acute dilatation of the stomach, diagnosed and relieved by gastric lavage (p 1743) With intestinal obstruction and all other conditions associated with tympanites In generalized peritonitis with inflammation of undersurface of diaphragm Consider abdominal puncture or laparotomy (p 1920)
Diaphragmatic	With diaphragmatic pleurisy Check physical findings with chest x ray

suspected and the probability is investigated by injecting fluid into a guinea pig (p 62) or obtaining sections of the involved membrane

Adhesive Peritonitis —Adhesive peritonitis very rarely produces clinical manifestations that require surgical intervention At autopsy and on the operating table adhesions are often found but they rarely give rise to clinical afflictions despite the frequency with which patients report that their abdominal distress follows upon adhesions

The presence of peritoneal adhesions becomes dramatically manifest only when they produce an *intestinal obstruction* (p 1873) Under these

circumstances the clinical picture is that of the mechanical disturbance At operation the obstructing adhesion is found and separated Often no other surgical therapy is required provided that the involved loop of bowel is viable

Proliferative Peritonitis (Pick's Disease Polyserositis) —Proliferative peritonitis is an obscure and rare disorder that masquerades under various appellations The variety described by Pick consists of a *polyserositis* with involvement of *pleura pericardium* and *peritoneum* The pericardial lesion often results in a constrictive type of disorder with the characteristic circulatory manifestations (p 1011) Pick s disease is associated with *hepatic cirrhosis* (p 1069) At autopsy or operation the liver and spleen are found coated with a thick capsule which is best described as a 'sugar coating'

The origin of proliferative pericarditis remains obscure *Treatment* is ineffective except when *pericardiolysis* is performed (p 1011) for the relief of tamponade (p 872)

Peritoneal Carcinomatosis

Neoplastic infiltrations of the peritoneum are invariably metastatic Most often, the primary lesion is in the stomach ovary or large bowel

Peritoneal carcinomatosis becomes manifest as an effusive *ascites* or through the discovery of nodular painless *masses* Often the *liver* is enlarged and the hobnailed edge is palpable The diagnosis is established through histological examination of the aspirated ascitic fluid or through biopsy of material obtained at exploratory laparotomy

Aside from the mechanical relief which can be given by a *paracentesis abdominalis* (p 1920) little can be done to prevent an imminent fatal outcome Ovarian implantations respond for a time to x ray irradiation therapy

Torsion of the Omentum

Torsion of the omentum occurs with less frequency than might be suggested in view of the pendent and vulnerable situation of this structure

At times the omentum becomes involved in a hernial sac where it becomes incarcerated and strangulated but occasionally a torsion occurs without the latter circumstance The patient complains of abdominal pain with rigidity and vomiting At operation performed for an unknown type of intra abdominal accident, the lesion is discovered and readily remedied by excision of the involved structure

Fat Necroses of Omentum

See *Acute Pancreatitis* (p 1939)

Mesenteric Thrombosis

See p 1844

CHAPTER 96

THE PANCREAS METHODS OF EXAMINATION AND MONO TREATMENT CLINICAL DISTURBANCES

The pancreas is situated in the retroperitoneal area and rests on the posterior abdominal parietes It is inaccessible to the ordinary methods of physical examination and cannot be delineated by special technics Despite its physiological importance methods are lacking to detect any but the grossest abnormalities except for disturbances of the internal secretion of the islands of Langerhans These are more properly considered in the section on *Diseases of the Endocrine Glands* (p 1237)

The present material deals with the external glandular activities of the pancreas which constitutes a most unsatisfactory chapter in the practice of medicine Fortunately significant clinical abnormalities of these aspects of pancreatic disease are rarely encountered

PHYSIOLOGY

The pancreas yields *internal* and *external* secretions the latter pass by way of the duct system to enter the duodenum (p 3562)

Insulin —The principal internal secretory function of the pancreas is the formation and secretion of insulin (p 1237) hypersecretory disturbances which usually accompany adenomas of the pancreas result in episodes of hypoglycemic shock, elsewhere described (p 1243) hypoinsulinemia leads to the frequently observed condition of diabetes mellitus

Lipocaic —There is an increasing awareness of the relationship of the pancreas to the metabolism of the *lipids* An internal secretion tentatively named *lipocaic* may be related to the *lipoidoses* and the intractable dermatosis of *psoriasis*

External Secretion —The external secretion of the pancreas contains a group of enzymes which aid in the digestion of protein carbohydrate and fat The most important of the specific substances are (1) *steapsinogen* activated to steapsin by bile (2) *trypsinogen* activated to trypsin by enterokinase (3) *diastase* an amylolytic ferment which participates in the digestion of the starches and (4) pancreatic *lipase* concerned with the metabolism of the fats

The pancreatic external secretion is controlled by *secretin* a hormone formed within the duodenal mucosa by the action of the hydrochloric acid of the stomach The sequence of events in this beautifully integrated mechanism, involves (1) the secretion of the acid by the stomach (2) propulsion of the gastric chyme into the duodenum where the mucous membrane is stimulated to form secretin and (3) a resultant outpouring of pancreatic secretion laden with enzymatic material for the digestion of protein starch and fat

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FAT NECROSES OF OMENTUM

See *Acute Pancreatitis* (p 1939)

MESENTERIC THROMBOSIS

See p 1844

no clinical value Patients with pancreatic insufficiency solve the problem of starch metabolism more readily by utilizing a diet containing a soluble sugar such as dextrose

Whole fresh pancreatic juice in concentrates or extracts is available only to a limited degree Its administration seems of value in animals who have an experimental isolation of the pancreas Clinically the preparation is inaccessible in amounts adequate to be of any therapeutic value

Lipocaic is an alcoholic extract of whole pancreas It is probably a hormone and may be an important element in the maintenance of normal fat metabolism Its principal function is that of preventing or removing hepatic deposits of fat which occur in animals that have had an experimental pancreatectomy and who have been adequately supplied with insulin Lipocaic promises to be of value in the treatment of the lipoidoses and perhaps also in psoriasis (p 3414)

Surgery.—The surgical treatment of pancreatic disease is most unsatisfactory Only in the instance of *adenomas* (p 1243) producing hyperinsulinemia is there any prospect of a satisfactory result from direct surgical procedure Occasionally pancreatic conditions are alleviated indirectly by present chapter Congenital fibrocystic disease appears elsewhere (p 2785)

CLINICAL DISTURBANCES OF THE PANCREAS

The following clinical disturbances of the pancreas are presented in the present chapter Congenital fibrocystic disease appears elsewhere (p 2785)

- Pancreatic Insufficiency
  - Celiac Disease (Congenital Steatorrhea)
  - Nontropical Sprue
- Acute Pancreatic Necrosis
- Chronic Interstitial Pancreatitis
- Cysts of the Pancreas
- Adenoma of the Pancreas
- Carcinoma of the Pancreas
- Pancreatic Lithiasis

PANCREATIC INSUFFICIENCY

Pancreatic insufficiency becomes manifest in early childhood as celiac disease in the adult it appears as nontropical sprue (p 1938) The etiology and pathogenesis of these conditions are not wholly clear since their manifestations do not occur solely from simple obstruction of the pancreatic ducts There is obviously some accessory causative factor that is responsible for the production of symptoms The problem is further confused by the fact that the resultant diarrhea produces superimposed metabolic disturbances such as deficiencies of protein calcium and vitamins

CELIAC DISEASE (CHRONIC INTESTINAL INDIGESTION CONGENITAL STEATORRHEA PANCREATIC INFANTILISM)

Celiac disease is a congenital disorder which usually becomes manifest in the second six months of life and is only rarely experienced after the sixth birthday Congenital fibrocystic disease (p 2785) appears within the first year

Clinical Manifestations —The child afflicted with celiac disease first shows irritability and then develops anorexia nausea and abdominal pain It is noticed that the youngster fails to gain weight and is pale and weak

The Pancreatic Ducts in Relation to the Biliary Passages—The discharge of pancreatic fluid into the duodenum occasionally occurs by a separate orifice but more often through a common channel with the bile Alterations in the mechanism of bile flow may result in a *reflux* into the pancreatic ducts and subsequent pathologic disturbance in the glandular tissues Infections of the biliary passages *may spread* by *continuity* into the pancreatic radicles Most thoughtful abdominal surgeons examine the pancreas during the course of operations on the biliary passages and are impressed by the high incidence of associated pancreatic damage

METHODS OF EXAMINATION

Attempts are made to investigate the pancreas by abdominal palpation and chemical *investigations of the ferments in stool urine duodenal contents* and blood

Abdominal Palpation—Except for the presence of a *huge tumor* in the abdomen situated centrally or to the left of center there are no physical methods by which lesions of the pancreas are suggested

Pancreatic Ferments—The pancreatic ferments are examined in the *duodenal content* (p 3726) or the *stool* (p 3728) In neither instance are changes reflected unless there is a gross and almost complete interference with pancreatic secretion Under these circumstances the feces may exhibit the characteristics of pancreatic insufficiency (p 1937) The stool is bulky with *creatorrhea* (undigested muscle fibers), *azotorrhea* and *steatorrhea* (unabsorbed fat)

Blood and Urine Amylase—Studies of blood amylase (p 588) have been utilized in an attempt to discover a reliable diagnostic procedure for the early recognition of acute pancreatic lesions The amylase levels of blood and urine often rise sharply in the first twelve to twenty four hours of acute pancreatic duct obstruction These findings are of value in patients with acute upper abdominal pain suggesting a surgical emergency Unfortunately the test is available only in the larger laboratories and is not wholly consistent and reliable

Secretin—The external secretion of the pancreas is normally *increased* by the intravenous injection of Hammarsten s secretin or the intraduodenal instillation of 2 to 3 cc of ether The patient is intubated with a duodenal tube and pancreatic flow commences several minutes after the injection or instillation and amounts to about 150 cc in an hour

SPECIAL METHODS OF TREATMENT

The approach to the treatment of pancreatic disorders is by surgical intervention or administrations of extracts

Pancreatic Extracts—The external secretions of the pancreas are available in active form though they possess little therapeutic efficacy The use of insulin (p 1237) is described in the chapter on endocrinology lipocaic is still an experimental preparation

Pancreatin U S P is an example of a pharmacologically active and therapeutically feeble substance The extract contains lipase diastase and trypsin and is administered in enteric coated tablets and powders The recognized dose is 0 5 to 1 0 gm (7½ to 15 grains) If enormous *daily doses* (25 to 50 gm) are *given* it is sometimes possible to relieve pancreatic diarrhea but little else is accomplished

Diastase is an active amylase that is commercially available *Though* promoted enthusiastically by pharmaceutical manufacturers *diastase* is of

Clinical Manifestations—The patient gives a more or less colorless history of anorexia loss of weight and strength and diarrhea In the early stages the diagnosis rests upon the examination of the stools which disclose undigested meat fibers (*azotorrhea*) and undigested fat (*steatorrhea*) Staining reactions reveal that the bulk of the fat is in the nature of neutral fat or fatty acid An exhaustive investigation fails to reveal any other cause for the diarrhea such as amebiasis bacillary dysentery or helminthiasis Roentgenologic examination shows no tangible abnormality The blood sugar fails to rise in the normal fashion following the dextrose meal (p 714) blood and urine diastase may be increased indicating some insufficiency of the external pancreatic secretion injections of secretin fail to stimulate an outpouring of pancreatic juice

With increase or persistence of steatorrhea deficiency manifestations become apparent An *anemia* develops which may be of the *hyperchromic type* (p 1077) suggesting a pernicious anemia the vitamin deficiencies produce *stomatitis* and *glossitis* the latter adding to the resemblance to pernicious anemia Hypoproteinemia results *in a generalized edema* and calcium deficiency may cause *disturbances of bone* and *tetany* (p 723)

The metabolic complications are cumulative and the patients often develop in the terminal stages ulceration involving the ileum and colon suggesting the psychosomatic manifestations of regional ileitis and chronic nonspecific ulcerative colitis (p 1850) Unchecked the course is progressively downhill and death occurs in almost one third of those afflicted

Treatment—The treatment of nontropical sprue is very similar to that employed in celiac disease in infancy (p 1938) A high protein diet (p 674) is ordered the patient is encouraged to eat ripe bananas and fresh strawberries calcium is added to the protein or lactic acid milk and a multivitamin preparation is given with each feeding hydrochloric acid (p 1740) is taken before and during meals pancreatic extract is prescribed in doses of 25 to 50 gm daily If fresh pancreas can be obtained from the slaughter house it is eaten after being lightly broiled Liver extract is injected whether or not an anemia is present

As soon as the patient is convalescent an attempt is made to seek out the fundamental disturbance Organic lesions such as pancreatic calculi and diseases of the biliary passages may warrant surgical intervention psycho emotional difficulties need the most skillful ministrations a hypoglycemia calls for the exhibition of insulin (p 1237)

ACUTE PANCREATIC NECROSIS (PANCREATIC APOPLEXY)

Acute pancreatic necrosis is a dramatic and serious abdominal catastrophe It may be caused by a variety of mechanisms such as trauma epidemic parotitis mechanical obstruction of a larger or smaller pancreatic duct or a vascular accident (pancreatic apoplexy)

Pathology—The anatomic changes in pancreatic necrosis vary between a mild edema as seen in the early stages at operation to the gangrenous lesion observed at autopsy A particularly important and pathognomonic finding at operation is the appearance of multiple foci *of fat necrosis* distributed in the panniculus and over the omentum These areas are small opaque lesions which appear like a flicked cigarette ash They result from the effects of the lipolytic ferments which have escaped from the pancrea

In early examples physical examination reveals distention of the abdomen despite weight loss and characteristic large fatty stools leaving greasiness about the anus

Microscopic examination of the feces shows undigested meat fibers (*creatorrhea azotorrhea*) and *steatorrhea* (unabsorbed fat) Fats are best demonstrated by staining a thin layer of feces with Nile blue sulfate prepared by dissolving 0 1 gm with 1 cc of glacial acetic acid in 100 cc. of distilled water *Neutral fats* which may make up to 70 to 90 per cent of the stool content are colored a light red the *partially split fats* are violet the *fatty acids* are blue and the *neutral calcium salts* remain a clear transparent white

If the manifestations of celiac disease persist for any length of time deficiency states are superimposed Inadequate absorption of vitamins leads to the production of *glossitis* and *stomatitis* through lack of vitamin B complex, evidences of *rickets* appear through lack of vitamin D hypocalcemia causes *osteoporosis* with frequent *fractures* and *tetany* *anemias* are commonly observed and may be of the hyperchromic type hypoproteinemia results in a *generalized edema,* most marked in the legs and face The general metabolic breakdown is attested by failure of growth and the appearance of a complete picture of *pancreatic infantilism* (p 2785)

Treatment—*Celiac disease is effectively treated by a high protein diet* (p 674) The most important food constituent is a protein or lactic acid milk each quart of which is fortified with 50 to 75 gm of calcium caseinate and 85 gm of banana powder Some children thrive on the banana powder alone and others are able to digest mashed raw bananas Multivitamin preparations are given before each feeding and injections of liver extract are made for relief of the anemia

As soon as appetite returns a schedule of frequent feedings is introduced A high protein intake is maintained by the addition of meat cottage cheese and egg white The vitamins are liberally supplied in orange juice and cod liver-oil preparations

Not until the child has been relatively symptom free for at least six months should carbohydrate be introduced A small amount of bread or cereal is tentatively added If this is well tolerated the portion is increased and a similar trial made with another variety of starch

PANCREATIC INSUFFICIENCY IN THE ADULT (PSILOSIS NONTROPICAL SPRUE IDIOPATHIC STEATORRHEA)

Pancreatic insufficiency in the adult is very similar to celiac disease in the infant Some of those afflicted have *demonstrable organic disease* such as cirrhosis of the liver chronic suppuration in the biliary passages pancreatic calculi chronic interstitial pancreatitis or a neoplasm involving that organ *In other patients the disturbances arise under circumstances which* suggest a *psychosomatic mechanism* (p 1344) The patient is often a young woman or an older spinster There is a history of a prolonged emotional strain or depression There are evidences of 'autonomic imbalance The patient complains bitterly *of alleged food intolerance and one food after* another is avoided until a deficiency diet of a monotonous type remains

As with celiac disease the original syndrome is soon obscured by the presence of symptoms relative to the vitamins calcium and iron deficiency

ical practice and are useless after the first day of the illness since they return to normal

Course —Systematic observations of serum amylase indicate that mild attacks of acute pancreatitis occur more often than is generally suspected These may eventuate in the condition of *chronic interstitial pancreatitis* (p 1941) or more rarely present the fulminating manifestations described above

Acute hemorrhagic pancreatitis often terminates fatally within twenty four to forty eight hours after onset In more favorable examples the acute manifestations subside and the patient goes on to develop a localized pancreatic abscess or cyst A fair proportion of patients are subjected to laparotomy with the institution of drainage down to the local area

Treatment —The efforts of the practitioner are immediately directed to the treatment of vasomotor collapse and shock A continuous *intravenous infusion* is established with the addition of *plasma* as soon as the substance can be obtained Meanwhile the surgical consultant is summoned and attempts are made to obtain sufficient improvement in the general condition so that a laparotomy can be attempted

Any operative interference attempted during the stage of shock is almost invariably fatal Later if the condition is recognized the abdomen is opened and drains are placed down to the involved structure

If the patient has the good fortune to recover roentgenologic studies are made to elucidate the nature of the more fundamental disturbance such as the presence of pancreatic calculi or abnormalities in the gallbladder or its duct systems Secondary operation may be required to remove the prime cause or drain a resultant pancreatic cyst or abscess

Chronic Interstitial Pancreatitis

Chronic interstitial pancreatitis is frequently observed by surgeons who make it a practice to palpate the gland during the course of procedures involving the biliary structures An induration is reported suggesting malignancy but biopsy shows merely a diffuse sclerosis with some atrophy of the parenchyma

Clinical Manifestations —Chronic interstitial pancreatitis produces amazingly few clinical manifestations Patients with demonstrable histological lesions may recall recurrent attacks of abdominal pain localized in the epigastrium Occasionally they report radiation to the left costal margin or the angle of the left scapula Tenderness may be elicited in the painful region or over the lower thoracic or upper lumbar spine suggesting the presence of a *spondylitis* (p 2915 2850)

The attacks may be accompanied by a low grade fever After an initial increase in the early attacks the levels of blood and urine amylase are no longer elevated If the insular tissue is destroyed the patient develops the symptoms and chemical signs of a *diabetes mellitus* (p 1246) Occasionally with cyst or abscess formation a mass is noted whose nature is revealed at laparotomy

Treatment —The treatment of chronic interstitial pancreatitis is thoroughly unsatisfactory A bland diet is ordered and the patient is given sedation If obvious disease is observed in the biliary tract or a palpable

and into the peritoneal cavity Autodigestion of protein tissue also occurs and may be partially responsible for the extensive hemorrhage and shock

Experimentally the injection of bile into the pancreatic duct reproduces the lesion of the acute pancreatic necrosis It is suggested that a similar mechanism is operative in man and may follow upon increased intrabiliary pressure with a reflux into the pancreatic system

Clinical Manifestations —The clinical manifestations of acute pancreatic necrosis are sudden and violent The patient is seized with such *agonizing abdominal pain* that he is unable to provide any information or description of his discomfort Examination reveals marked *tenderness* and *rigidity* of the entire abdomen There are manifestations of extreme *vasomotor collapse* and *shock* Later a *blue discoloration* may be observed in the region of the umbilicus or along the lateral aspects of the thighs



Fig 449 —Pancreatic fat necrosis in the omentum *

In the majority of instances it is suspected that there has been a rupture of a hollow viscus At operation the areas of fat necrosis furnish the first suspicion of the nature of the disturbance and direct the attention of the surgeon to the region of the pancreas

On rare occasions the diagnosis is suspected preoperatively due to the occurrence of the episode during an attack of *epidemic parotitis* (p 480) or in a patient with known gallbladder disease If it is possible to obtain determinations of the blood and urine amylase a marked elevation is noted within the first twenty four hours These tests are rarely available in clin

* MacCallum Textbook of Pathology

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DIFFERENTIAL DIAGNOSIS OF

Pain in the Left Upper Quadrant

Pain in the left upper quadrant may be most deceptive since *in addition to involvement of the underlying stomach and spleen it may be caused by supradiaphragmatic lesions of* pleura lungs and heart

SITE	DIAGNOSTIC FEATURES
Parietes	
Intercostal Neuralgia	Usually of herpetic origin with early hyper algesia and later development of characteristic vesicle (p 435)
Slipping Rib	*With sharply localized pain and tenderness at the* costochondral junction. Relieved by pro caine injection (p 3915)
Respiratory Tract	With lobar pneumonia pneumonitis or pleur isy involving lower lobes Check physical findings with chest x ray
Circulatory and Hematopoietic Systems	
Fibrinous Pericarditis	With characteristic friction rub
Angina Pectoris	Relieved by nitroglycerin (p 890) Normal Ecg
Coronary Insufficiency or Occlusion	Unrelieved by nitroglycerin May be accom panied by shock leukocytosis and increased sedimentation rate Characteristic Ecg (p 983)
Splenic	Perisplenitis associated with splenomegaly and splenic infarction Get hemogram for blood dyscrasias (p 1085) and blood culture for pos *sible subacute bacterial endocarditis (p 1021)* With ruptured spleen requiring laparotomy
Digestive Tract	
Gastric	With peptic ulcer gastric neoplasm or cas *cade stomach (p 1805) Obtain gastric con tents (p 3722) Make repeated examinations* of stool for blood (p 3728) and perform barium meal
Colonic	*Particularly gaseous distention of splenic flex* ure Malignancy of splenic flexure Make repeated examinations of stool for occult blood (p 3728) Perform barium meal and enema (p 1824)
Pancreatic	*Cysts and malignancy of tail of pancreas* Consider exploratory laparotomy (p 1943)
Urinary Tract	Carbuncle furuncle and perinephric abscess Hydronephrosis pyonephrosis and calculus of left renal pelvis or ureters *Examine urine for* red cells and leukocytes (p 3683) Get scout film for radiopaque shadows (p 2250) Consult specialist for retrograde and intra venous pyelograms (p 2251) and cystoscopy (p 2248)

mass is noted in the region of the pancreas laparotomy is justifiable with the correction of the pathologic conditions which present themselves to the surgeon Needless to say the exploration must include a wide exposure of the common duct

Cysts of the Pancreas

Pancreatic cysts may be *congenital* but more often they result from *trauma* such as blows or repeated constant pressure they may be produced by attacks of *acute hemorrhagic pancreatitis* (p 1939) or *chronic interstitial pancreatitis* (p 1941)

The first symptom in these rare circumstances is the observation of an *epigastric tumor* (p 1814) The patient may give a preexistent history of an attack of acute hemorrhagic pancreatitis or there may be repeated complaints suggesting a chronic interstitial pancreatitis Associated pathologic changes are often demonstrable in gallbladder and biliary passages At times evidences of insular compromise are afforded by the presence of hyperglycemia and glycosuria

Laboratory investigations particularly roentgenologic examination are remarkable for their negativity Exploratory laparotomy reveals the nature of the mass which may be drained and marsupialized

Adenoma of the Pancreas

Adenomas of the pancreas usually involve the *islands of Langerhans* They are recognized by the attacks of *hypoglycemic shock* due to hyperinsulinism elsewhere described (p 1242) The adenomas may be surgically removed with gratifying amelioration of symptoms

Cancer of the Pancreas

Cancer of the pancreas which is fortunately of rare occurrence is difficult of diagnosis In most instances the neoplasm is derived from the exocrine cells Rarely the malignancy arises in the cells of the islands of Langerhans and produces the clinical syndrome of hyperinsulinism (p 1242) The growth may be present in the head or the tail of the organ

Carcinoma of the Head of the Pancreas—Carcinoma of the head of the pancreas occurs more frequently in males It may be adenocarcinomatous or scirrhous Regional metastases occur to liver and lymph nodes

The symptoms of cancer of the head of the pancreas are most insidious The patient notes local *pain loss of weight* and *jaundice* Examinations are completely normal unless a nontender distended *gallbladder* (Courvoisier) becomes palpable Strangely enough despite the absence of biliary and pancreatic secretion in the duodenum there are no evidences of pancreatic insufficiency such as those described with celiac disease or nontropical sprue in adult life (p 1938)

Carcinoma of the Tail of the Pancreas—Cancer of the body or tail of the pancreas is generally accompanied by excruciating *local pain* that is independent of motion or meals It is distributed in the upper abdomen or lower thorax and occasionally referred to the lumbar region of the spine There may be a sudden appearance of manifestations of *diabetes mellitus Splenic*

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CHAPTER 97

THE LIVER: TESTS OF LIVER FUNCTION CLINICAL DISTURBANCES

ANATOMY

THE gross anatomy of the liver is elsewhere described (p 3558) A comprehensive understanding of the physiology and clinical disturbances of hepatic tissues requires a preliminary review of their blood supply the architecture of the liver lobule and the reticulo endothelial system

The Blood Supply —The liver lobule possesses a unique vascular organization hepatic tissue receives an *arterial inflow* from the hepatic artery and a *venous inflow* from the portal vein The *outflow* of blood is collected in the radicles of the hepatic vein which then empties into the inferior vena cava

The *hepatic artery* behaves as any other nutrient vessel it contributes only one-quarter of the total blood supply but furnishes about half of the oxygen requirements necessary for the manifold activities of the parenchymal cells The *portal vein* which has a diameter 8 to 10 times larger than the hepatic artery collects venous blood from the splanchnic area it is heavily laden with the products of digestion and transports about 75 per cent of hepatic blood volume It enters the liver lobule at its periphery and divides into smaller *interlobular veins* and capillary like *hepatic sinusoids*

The hepat c sinuso ds are the terminal divis ons of the portal system they lie between the liver cords a d are separated from b le cap llaries by single layers of hepatic cells they converge toward the center of the lobule in the manner in which the spokes of a wheel pproach the hub they un t to form the *central veins* wh ch traverse the liver lobule in

enlargement occurs when venous thromboses are induced by the neoplasm *Jaundice* is present as a terminal manifestation

Diagnosis—The diagnosis of cancer of the pancreas is rarely made before operation or autopsy unless the Courvoisier gallbladder is apparent at an early stage Under other circumstances the practitioner is driven to an exploratory laparotomy and the growth is first revealed at operation A *biopsy* is required since the mere palpatory induration may turn out fortunately to be an evidence of a chronic interstitial pancreatitis (p 1941)

Treatment—Cancers of the head of the pancreas are reported to have been successfully extirpated together with the duodenum on rare occasions This procedure should not be attempted except by a surgeon of great skill and experience It is better to create a palliative biliary fistula and prevent the discomfort of cholemia (p 1953)

CALCULUS OF THE PANCREAS

Pancreatic lithiasis is a rare condition that is usually revealed at exploratory laparotomy or autopsy Stones are usually numerous and are composed of a nucleus of *calcium carbonate* and *calcium phosphate* When they are of sufficient size they may be demonstrable by radiography

Pancreatic lithiasis rarely causes demonstrable symptoms Occasionally the patient notes pain following meals If this is associated with a fatty diarrhea (p 1938) the condition may be suspected and proved by the scout film

The impaction of the pancreatic stone may cause a dilatation in the gland chronic interstitial inflammation or an acute suppurative pancreatitis Because of these possibilities *operative removal* is advisable

26 The production of the erythrocyte maturation factor (liver extract)
27 The manufacture of heparin
28 The regulation of the acid base equilibrium of the blood
29 An important source of blood heat
30 Through the distensibility of its sinusoids the liver is important in the regulation of the blood volume
31 In the embryo the liver functions for hematopoiesis
32 The synthesis of hippuric acid
33 The synthesis of uric acid

The Kupffer Cells.—The Kupffer cells in common with the remainder of the reticulo-endothelial system function for the *formation of bile pigment* (p 1985) they filter colloidal material that has entered the circulating blood they phagocyte *iron* that has been liberated from the breaking down of hemoglobin they have great importance in *antibody formation* and the *processes of immunity* (p ˜3)

TESTS OF LIVER FUNCTION

It requires only a cursory knowledge of the multiplicity of hepatic functions to realize that there can be no such thing as a single test of liver activity The sinusoids may be engorged with blood as the result of circulatory failure without serious impairment of the metabolic activities of the liver cells disturbances in the prehepatic mechanisms of bile formation and posthepatic bile excretion are possible without significant or commensurate dislocation of the other activities of the parenchyma there may be partial injury as seen in liver abscess or neoplasm yet there is abundant active tissue to carry on without an appreciable disturbance of bodily efficiency

The specific tests of liver function measure excretory and metabolic activities

Excretory Liver Function Tests

The excretion of bilirubin in the bile is a basic hepatic function Normally the concentration of this pigment in the blood is low usually from 0 1 to 1.5 mg per 100 cc Any increase in the concentration produces jaundice which is due to biliary obstruction (retention) or to failure of the liver to excrete bilirubin Bilirubin concentration may be estimated by the quantitative *Van den Bergh reaction* which is a complicated procedure or by the *icterus index*

Van den Bergh Reactions.—The Van den Bergh reactions are based on the interaction of Ehrlich s diazobenzolsulfochloride with bilirubin The reaction occurs in two principal forms the indirect requiring the addition of alcohol and the direct occurring without alcohol This difference depends on the physicochemical state of plasma bilirubin which varies with the mechanism of the jaundice

The *indirect reaction* occurs after 0.25 cc of Ehrlich s reagent is added to 1 cc of the supernatant portion of a centrifuged mixture of 1 cc of serum and 2 cc of 95 per cent alcohol The supernatant fluid is a clear reddish violet solution of *azobilirubin* When the color is fully developed it is compared colorimetrically with the Van den Bergh standard solution of anhydrous cobaltous sulphate (2 16 gm per cent) The color of the standard is equal to that of one unit of bilirubin (1 to 200 000 solution)

The *direct reaction* occurs with the addition of 1 cc of the reagent to 1 cc of serum It may be (1) *immediate* a violet color appearing within

the manner of the wheel's hub The central veins give into *sublobular* and *hepatic veins* eventually emptying into the *inferior vena cava* and the *right auricle*

The Liver Lobule—The morphology of the liver lobule is best considered with reference to its extraordinary vascular arrangement Columns or cords of liver cells radiate from the central vein they are separated each from the other by the sinusoids which are remarkably distensible and serve as a *sluice mechanism* in the hemodynamics of the circulation (p 781) The blood that is contained within the sinusoids does not come into direct contact with the hepatic cells but a rich opportunity is afforded for osmosis and filtration

The secretory product of the hepatic cells is drained into the bile capillaries These with the branches of the portal vein and hepatic artery occupy a position at the periphery of the lobule where they are set in a connective tissue stroma The latter and the inter lobular septums receive their blood supply from the hepatic artery whose capillaries unite to form hepatic veins which empty into the inferior vena cava

The Reticulo endothelial System—The liver is richly endowed with reticulo-endothelial cells In the walls of the sinusoids are found the *phagocytic stellate cells of Kupffer* which are similar in function and morphology to the circulating *monocytes* (p 1010) and the *histiocytes* of connective tissue spleen lymph nodes bone marrow adrenal cortex pituitary glands and the central nervous system (microglia)

The reticulo-endothelial cells or histiocytes are *tissue macrophages* they are phagocytic for foreign particles of all types particularly those of large dimension that cannot be handled by the polymorphonuclear neutrophils or the microphages *Histiocytes possess the quality of vital or supravital staining* when exposed to weak solutions of *trypan blue* and *lithium carmine*

PHYSIOLOGY

The liver is the largest organ of the body it has the greatest variety of functions the widest margin of safety and the most amazing ability to regenerate after damage So great is its complexity that for present purposes it is possible only to enumerate the manifold activities of the hepatic and Kupffer cells

The Hepatic Cells—The more important functions of the hepatic cells include

1 The manufacture of glycogen from glucose lactic acid and certain of the amino acids (*glycogenesis*)
2 The storing of glycogen in the liver lobules
3 The liberation of glycogen (*glycogenolysis*) when needed to maintain the level of the blood sugar
4 The conversion of glucose and protein into fat
5 The storage of protein
6 The synthesis of certain of the amino acids the intermediate metabolism of the amino acids elevation of metabolic rate (specific dynamic action of protein) due to increased energy liberated by hepatic cells during protein utilization
7 The desaturation of the fatty acids
8 The production of organic acids such as beta hydroxybutyric acid
9 The conversion of carotene into vitamin A
10 The storage of vitamin A
11 The storage of vitamin D
12 The storage of vitamin K
13 The storage of vitamin B complex
14 The synthesis of urea by the deamınization of amino acids
15 The production of plasma protein
16 The production of plasma albumin
17 The production of plasma globulin
18 The production of fibrinogen
19 The production of prothrombin
20 The storage of iron and copper
21 The secretion of bile (p 1985)
22 The excretion of bile (p 1986)
23 The synthesis of cholesterol and its ester
24 The production of the bile salts
25 The detoxification of blood from chemical substances and particulate matter Chemical detoxification occurs by conjugation oxidation reduction a cetylation

impaired hepatic function Normally urobilinogen is present in dilution of 1 20 Increases indicate hepatic impairment in the absence of increased blood destruction biliary tract infection or a large infarct

Metabolic Function Tests

Galactose Tolerance Test —The normal liver converts galactose into glucose which is stored as glycogen In the presence of liver disease this function is often impaired and if a quantity of galactose is given by mouth excessive quantities of galactose appear in the urine

Technic—Forty grams of galactose are given with the juice of two lemons in 500 cc of water to a patient who has fasted for twelve hours The urine is collected every hour for five hours The quantity of sugar in each specimen is determined with *Benedict s quantitative reagent* (p 3675) The total quantity of sugar is multiplied by 0 7 (1 gm of glucose equals 0 7 gm of galactose in reducing power)

Results—*Normally* the maximum excretion in five hours is 3 gm Anything over 5 gm indicates liver damage The absence of galactosuria does not rule out liver damage The test can be performed in jaundiced patients

Gluco e Tolerance Test.—The rapidity with which the liver removes an excess of sugar from the blood is often a measure of liver function The damaged liver fails to do this normally and there is an abnormal rise in the blood sugar after a known amount of glucose by mouth The *technic* of this test has been described (p 3716) Abnormal results require differentiation from diabetes mellitus and other causes of disturbed glucose tolerance

Cholesterol Partition —The ratio of the total and esterified cholesterol affords valuable data regarding the state of liver function in jaundiced patients In all forms of hepatic degeneration there is a tendency for the cholesterol ester concentration to drop while the total cholesterol may be high or normal In severe cases the esters may disappear from the blood (normal 60 to 70 per cent) Serial determinations of the ester fraction enable the observer to detect the progress of a seemingly mild hepatitis going on to acute yellow atrophy

Takata Ara Reaction.—In liver disease particulary *cirrhosis* there is often an increase in the serum globulin concentration When such serum is added to a mercuric chloride solution a white cloud is formed The intensity of the reaction varies roughly with the degree of hyperglobulin emia The test is not specific for liver disease A similar reaction known as the *formol gel test* is performed by adding 2 drops of 40 per cent formalin to 1 cc of serum In the presence of an increased serum globulin the serum will jell almost immediately

Hippuric Acid Synthesis (Quick)—The ability of the liver to convert sodium benzoate into hippuric acid is measured by injecting intravenously a solution of 1 77 gm of sodium benzoate in 20 cc of sterile distilled water Urine is collected at the end of one hour

A normal adult without renal impairment excretes at least 1 gm of hippuric acid in one hour The test is regarded by those who use it widely as a delicate indicator of hepatic efficiency in jaundiced and nonjaundiced patients

20 seconds (2) *delayed* a red color deepening into violet after one minute or (3) *biphasic* a red color slowly deepening into violet

The explanation of the various types of Van den Bergh reaction advanced by Barron hypothesizes that bilirubin normally exists in plasma as a bilirubin globulin complex This combination prevents excretion of bilirubin into urine or spinal fluid and produces the direct diazo reaction Alcohol breaks up the pigment protein complex freeing bilirubin which gives the indirect reaction when the production of bilirubin outstrips the capacity of the liver cells to excrete it

The direct reaction depends on the retention of bile salts and cholesterol along with bilirubin The salts lower surface tension and prevent the formation of the bilirubin globulin complex Free bilirubin being a free small molecule is readily diffusible and appears in the urine and tissues when the renal threshold of 2 to 3 mg per cent is exceeded The *biphasic* reaction is due to the presence of both free and combined bilirubin in the plasma

Icterus Index—The icterus index is determined by comparing the color of the serum and a standard 1 10 000 solution of potassium bichromate in a colorimeter The reading of the standard divided by the reading of the serum is the icterus index Values up to 6 are *normal* higher indices indicate an increased amount of bilirubin in the blood The serum must be clear and not hemolyzed A high blood carotene concentration is a source of error producing high values There is no absolute correlation between the icterus index and the serum bilirubin concentration but because of its simplicity the test is a valuable criterion for following the severity of jaundice from day to day

Bilirubin Excretion Test—A sensitive test of the excretory capacity of the hepatic cells measures the rapidity with which a known quantity of injected bilirubin is excreted This test requires the careful preparation of the bilirubin solution which is quite expensive and facilities for the quantitative estimation of serum bilirubin

One milligram of bilirubin per kg of body weight is injected intravenously and blood samples are taken five minutes before and one half hour and four hours after injection The bilirubin concentration is determined for each sample

Retention of 5 to 6 per cent of the bilirubin at the end of four hours is the upper limit of normal This test is most delicate in the detection of slight degrees of hepatic function It is valueless in the presence of jaundice

Bromsulfalein Test—The excretory function of the liver may be tested by noting the rate of removal of bromsulfalein a dye excreted in the bile A definite quantity of the dye (2 mg per kg of body weight) is injected intravenously and the amount remaining in the blood stream after thirty minutes is determined by a colorimeter Normally the dye is removed in thirty minutes Retention of the dye indicates hepatic insufficiency

Instead of bromsulfalein another dye *rose bengal* may be used to test liver function The results are similar to those obtained with the first substance

Urinary Urobilinogen Excretion—The quantity of urobilinogen excreted in the urine reflects the functional state of the liver an increase indicating

are bile stained but there is rarely any evidence of hepatic insufficiency in the syndrome of liver death the patient may succumb to a cholemia without ever developing icterus

JAUNDICE (HYPERBILIRUBINEMIA AND BILIRUBINURIA)

Jaundice is the discoloration of body tissues caused by excessive amounts of bilirubin in extracellular fluids It is reflected clinically by the yellow tint of skin conjunctivae sclerae and oral mucous membranes The intensity of jaundice parallels the bilirubin concentration of blood plasma The amount of bilirubin present in plasma is determined by the intensity and rate of red blood cell destruction the functional capacity of the hepatic cells and the patency of the biliary radicals

Biochemical Aspects of Jaundice.—Bilirubin is a pigment derived from the porphyrin portion of the hemoglobin molecule It is produced in the process of red blood cell disintegration by the reticulo endothelial system One gram of hemoglobin yields about 40 gm of bilirubin Plasma normally contains from 0 1 to 0.5 gm per 100 cc

Bilirubin is removed from plasma by the hepatic parenchyma and is excreted in the bile In the intestine it is reduced by bacterial action to urobilinogen a colorless compound Some urobilinogen is reabsorbed into the portal circulation while the remainder is oxidized by bacteria to uro bilin the brown pigment of stool The reabsorbed urobilinogen is again excreted into the bile by the liver cells A small amount enters the urine where it is converted to urobilin The ability of the liver cells to remove urobilinogen and bilirubin from the blood is a sensitive index of liver function

Pathogenesis —Although jaundice occurs as a symptom of a wide vari ety *of clinical conditions the increase in plasma bilirubin is caused by one* or more of the three following basic mechanisms (1) Excessive blood de struction (hemolytic jaundice) (2) hepatic insufficiency (hepatogenous jaundice) and (3) obstruction of the extrahepatic biliary passages (ob structive or surgical jaundice)

Pre hepatic or Hemolytic Jaundice —Pre hepatic jaundice is essentially a disturbance in which the formation of bilirubin is excessive The increased production of biliary pigment follows on excessive hemolysis as in so called hemolytic jaundice The hemolytic types of jaundice are discussed in the section dealing with Blood Dyscrasias (p 1060)

Hepatic Toxic or Hepatogenous Jaundice —True hepatic jaundice re sults from insufficiency of the liver cells and it is usually caused by a toxic or an infectious process Hepatogenous jaundice is considered in the pres ent section with the material on *Toxic Hepatitis* (p 1963)

Post-hepatic Surgical or Obstructive Jaundice —Post hepatic jaundice results from mechanical obstruction of the extrahepatic biliary passages It is usually referred to as surgical jaundice It is associated with acholic stools and the differential aspects are tabulated on p 1952

Mixed Types of Jaundice —Pure examples of pre hepatic hepatic or post hepatic jaundice are rarely observed Pre hepatic or hemolytic jaun dice is invariably associated with a certain amount of hepatocellular in sufficiency The final clinical picture is usually that of combined pre hepatic and hepatic derangement. With *post hepatic or obstructive* jaun

Sodium *d* Lactate Test —To study the capacity of the liver to convert blood lactic acid into glycogen 70 mg per kg of body weight of a 14 per cent solution of sodium *d* lactate is injected intravenously in the resting fasting state Blood is collected before and thirty minutes after injection

In normal subjects less than 5 mg of the injected lactate remains in the blood at the end of one half hour Patients with hepatocellular jaundice show abnormal retention of injected lactate whereas those with extra hepatic biliary obstruction do not

Cephalin Cholesterol Flocculation Test —The serum of patients with hepatic parenchymal damage flocculates a colloidal suspension of a cephalin cholesterol emulsion This gives an accurate indication of parenchymal damage whether due to long standing obstruction or to toxic hepatitis

As is true of all tests of liver function and activity its interpretation requires insight into the possible causes of the phenomenon The test it self is not oracular It is of prognostic help since it indicates the actual damage to the parenchyma, whether during a clinically latent phase of cirrhosis or after prolonged extrahepatic biliary obstruction It was found not to give a single false positive test in normal individuals The test can not distinguish between extrahepatic and intrahepatic biliary obstruction

Serum Phosphatase —Determination of serum phosphatase activity offers information which is of supplementary value in the distinction between jaundice of extrahepatic biliary tract obstruction and the other types It is based on the fact that the liver excretes phosphatase into the bile Phos phatase in the blood is also derived from enzymatic activity in bone

Despite the difficulties in interpreting this test it is fairly well agreed that the serum phosphatase rises in gross biliary obstruction and is normal in toxic and hemolytic jaundice Combined cephalin and serum alkaline phosphatase tests are used in differentiating hepatogenous and obstructive jaundice High cephalin low phosphatase indicate hepatitis high phos phatase low cephalin obstruction no hepatitis Serum phosphatase below 10 units and a strongly positive cephalin test indicate that common duct *obstruction is improbable* Serum phosphatase over 10 and a negative cephalin test suggest extrahepatic obstruction

The normal range of serum phosphatase by the Bodansky method is 1 to 4 units per 100 cc of serum of the King Armstrong method between 3 7 and 13 1 units per 100 cc of serum

Prothrombin Time —Liver function also may be measured by determina tion of prothrombin time and the effects on the latter of injections of menadione (Vitamin K) Failure of the vitamin to adjust prothrombin time indicates severe hepatic damage

PATHOLOGIC PHYSIOLOGY

Hepatic dysfunction has a profound effect on the economy of the body as a whole Fortunately for the survival of the human race the liver has a tremendous margin of safety and a great capacity for regeneration In consequence *liver insufficiency* is rarely encountered and then usually as a *terminal event*

Injury to the liver cells may result in *jaundice* or the syndrome of *cholemia* These manifestations may be associated but each may appear in the absence of the other Thus in catarrhal jaundice (p 1973) the tissues

to infer that the liver cells have been injured and that the jaundice is obstructive However retention of liver function does not preclude the presence of cellular damage The late appearance of impairment of function may indicate liver damage from prolonged obstruction

The cephalin-cholesterol flocculation test is positive with liver cell damage but does not necessarily indicate impairment of function The serum phosphatase test suggests gross obstruction

Pre hepatic or Hemolytic Jaundice.—See p 1060

True Hepatic or Hepatogenous Jaundice —See *Toxic Hepatitis* (p 1063)

Post hepatic, Obstructive or Surgical Jaundice —Jaundice arises from obstruction to the flow of bile in the post hepatic biliary passages In most instances the hepatic parenchyma is functionally intact until later when in the presence of long continued obstruction infection and hepatic necrosis supervene The secretion of bile is suppressed when the pressure in the extra hepatic duct equalizes the secretory pressure of the liver cells Bile passes from biliary canaliculi through liver cells into the hepatic vein (regurgitation jaundice) Under these circumstances the liver enlarges as the result of engorgement of the biliary system constituting a hydrohepatosis Since the secretion of bile is suppressed substances which lower surface tension enter the blood in high concentration

Obstructive jaundice is usually intense and progresses to a greenish tint in chronic instances Pain is common and is usually of a colicky variety particularly when the obstruction is due to a calculus The presence of bile salts in the blood causes pruritus and bradycardia Xanthopsia may be encountered and chills and fever are associated with biliary tract infection

In an obstructive jaundice serum bilirubin is elevated the Van den Bergh test is directly positive the cholesterol and cholesterol esters are increased serum phosphatase reaches high values the cephalin flocculation test is negative the stool is bulky acholic fatty and has an offensive odor and the fat soluble vitamins (A D and K) are imperfectly absorbed as is calcium The result of these metabolic disturbances is a prolongation of prothrombin time a hemorrhagic tendency and osteoporosis (*hepatic rickets*) Bile pigment is present in the urine and may precede the recognition of clinical icterus by at least twenty four hours With complete obstruction urobilin is not present in the urine in excessive amounts With superimposed biliary tract infections bacteria may reduce large amounts of bilirubin to urobilin in the biliary system and there is thus produced a urobilinuria

CHOLEMIA

The minor manifestation of hepatic insufficiency commonly referred to as *biliousness* is discussed with the material on acute hepatic congestion (p 1056) *Cholemia* that occurs in association with *icterus* is described with the syndrome of *acute yellow atrophy* (p 1069) and *obstructive lesions* of the biliary ducts (p 2006)

Liver Death —The postoperative syndrome of liver death is an illustration of a fulminating instance of *nonicteric cholemia* Many surgeons are skeptical concerning its pathogenesis and incline to the belief that the derangement is a reflection of postoperative infection or significant damage to hepatic blood vessels

dice, the prolonged damming back of bile produces a certain amount of liver damage so that the final clinical manifestations are those of post hepatic retention and hepatic insufficiency True hepatic damage is partially due to insufficient removal of bilirubin from the circulating blood and an additional element of obstruction or post hepatic jaundice due to necrosis and edema permitting back diffusion or regurgitation of bile into the blood As the result, what begins as a pure hepatic defect partakes of the characteristics of pre hepatic and post hepatic involvement

The Validity of Laboratory Tests —Interpretation of laboratory tests in the diagnosis of jaundice is difficult, since no one method is oracular Each must be considered in conjunction with clinical findings and with the results obtained by other investigations

The *icterus index* (p 1948) indicates hyperbilirubinemia which is reflected clinically by the tint of the sclera Serial observations of the icterus index serve as an objective gauge to the course of events and indicate whether the process is receding or progressing

Van den Bergh tests are no more helpful than the icterus index Both direct and indirect methods may vary in a perplexing manner In the

TABLE 124 —LABORATORY AIDS IN THE DIFFERENTIAL DIAGNOSIS OF THE MECHANISMS OF JAUNDICE

	Pre hepatic	Hepatogenous	Post hepatic
Bilirubinuria	0	++	++++
Excessive Urobilinuria	++++	0*	0
Acholic Stools	0	0†	+
Anemia	+	0	0‡

* May be present in recovery phase
† May be acholic in severe forms
‡ May be present in obstructions due to malignancy

early stages of a true hepatic jaundice the Van den Bergh test is positive by the indirect method later as bile salts and cholesterol increase in the blood it becomes biphasic and then the immediate direct test is later obtained Furthermore the indirect test may be positive with small amounts of bilirubinemia and directly positive with large amounts regardless of the variety of the jaundice

Blood cholesterol is usually elevated in post hepatic or obstructive jaundice but there also may be increased amounts in hepatic jaundice particularly if there are disturbances of the finer bile canaliculi or when there is improvement in the damaged liver of a toxic hepatitis Anemia may be the result of a hemolytic process causing the jaundice but it may also follow a malignancy productive of obstruction and post hepatic jaundice

Tests of liver function such as the galactose tolerance and the hippuric acid synthesis indicate impairment of liver function without determination of the precise method by which the abnormality has been produced When these tests are positive early in the course of the jaundice it is fair

Choledochus Cysts	Usually in girls before the age of 10 Atypical shadow on cholecystogram (p 1994)
Cholesterosis	Strawberry gallbladd r without organic findings until organ is removed and opened (p 2005)
Acute Noncalculus Cholecystitis	With typhoid, colon bacillus or streptococcus bacteremia
Acute Calculus Cholecystitis	With radiographically demonstrable gall stones (p 1999)
Cholangitis Lenta	With bacteremia usually streptococcal
Hemolytic Icterus	With precipitation of bilirubin calculi
Toxic Icterus	As complication following edema and necrosis occluding biliary canaliculi

The acute syndrome becomes manifest when the patient develops stupor coma hyperpyrexia oliguria anuria and marked elevation of the nonprotein nitrogen of the blood This *hepatorenal disturbance* may be fatal within the course of a few days or a week Delayed instances are characterized by the later appearance of jaundice and its attendant phenomena

The *treatment* of postoperative cholemia is that of a toxic hepatitis (p 1963) but re exploration of the field is worthy of consideration At times a suppurative area may be drained and it may be possible to remove ligatures that inadvertently include a large artery or bile duct

CLINICAL DISTURBANCES OF THE LIVER

The clinical disturbances of the liver include congenital malformations mechanical lesions vascular abnormalities neoplastic disease metabolic derangements and infection

- Congenital Malformat ons
- Mechan cal Disturbances
  - The Corset Liver
  - R edel s Lobe
  - Hepatoptos s
- Vascular Distu bances
  - Hyperemia
  - Chronic Passive Congestion
  - Occlus on of the Hepat c Artery
  - Aneurysm of the Hepati Artery
  - Acute Thrombos s of the Portal Vein
  - Chronic Occlusion of the Portal Vein
  - Portal Hypertens on
  - Suppurative Pylephl b tis
- Neoplasms
  - *Benign Growths*
  - Primary Carcinoma
  - Primary Sarcoma
  - Metastatic Carcinomatosis
- Metabolic D sturbances
  - Toxic Hepat tis
  - Acute Yellow Atrophy
  - Subacute Red Atrophy
  - Portal Cirrhos s (Laennec
  - B l ary Cirrho is (Hanot

DIFFERENTIAL DIAGNOSIS OF

Obstructive Jaundice

Obstruction to biliary flow may be produced by mechanisms within the lumen of the duct stricture of the walls pressure on the ductal *system from without or functional* spasm as observed with contraction of the sphincter of Oddi as in biliary dyskinesia (p 2007)

	DIAGNOSTIC FEATURES
Choledocholithiasis	With stone in the common duct jaundice is usually intermittent and recurrent, and associated with attacks of chills and fever Look for radiopaque or radiotranslucent shadows in direct x ray and by cholecystography (p 2000)
Echinococcus Cysts	Note large palpable tumor eosinophilia positive skin test and ova or hooklets in stool
Cholangitis	Attacks of Charcot fever and paroxysms of deepening jaundice Temperatures to 104 F or more as ociated with chills
Neoplasms	Cancer of gallbladder bile ducts or pancreas Gradually deepening jaundice with distended painless gallbladder (Courvoi ier)
Chronic Pancreatitis	Findings as in malignant obstruction, verified only after laparotomy and biopsy (p 1941)
Strictures of Ducts	In congenital atre ia following operation post cholangitic and as the result of periduodenal and perigastric adhesions Exploratory laparotomy mandatory
Hepatic Distomiasis	In regions where liver flukes are encountered Look for ova in stools (p 1982)
Amebic Abscess	*In areas where amebic dysentery is encountered* Look for amebae in stools Note therapeutic response to emetine (p 525)
Multiple Liver Abscesses	Usually as the result of pylephlebitis following appendicectomy Note septic course and response to streptomycin and penicillin (p 106) Exploratory laparotomy indicated (p 1980)
Tertiary Syphilis	Obstruction by large gumma with positive serology and therapeutic response to iodide
Lymphadenopathy	Pressure or enlarged lymph nodes due to leukemia Hodgkin s disease or tuberculosis Get hemogram and lymph node biopsy (p 1136)
Portal Cirrhosis	In late stages with diminution in size of liver and ascites
Biliary Cirrhosis	In adolescence with fever enlargement of liver splenomegaly and clubbing of fingers
Hepatolenticular Degeneration	Wilson s disease in adolescence with hepatomegaly splenomegaly and neurologic manifestations
Biliary Dyskinesia	Attacks of biliary colic and jaundice without anatomic lesion. Relief from antispasmodics

clinicians and the laity speak of "biliousness" in reference to these disorders The *syndrome* consists of postprandial lethargy tenderness in the hepatic region and plethoric engorgement of the superficial vessels of head and neck

The accepted *treatment* of biliousness is the *calomel-saline* sequence (p 1831) Pharmacologists insist the mercurial has no demonstrable effect on liver function or the flow of bile but many clinicians and patients report a therapeutic action that seems to transcend mere mechanical purging

PASSIVE CONGESTION ("NUTMEG LIVER")

The liver serves as a protective reservoir against the overloading of the heart with blood derived from the portal system Congestion of the liver is observed in all types of *backward failure* (p 941) but most particularly

DIFFERENTIAL DIAGNOSIS OF

Swellings and Tumors in the Right Upper Quadrant

In the lean and particularly ptotic individual it is often possible to palpate the edge of the liver and the lower pole of the right kidney in health. The presence of swellings and tumors over and above these normal abnormalities requires intensive investigation with radiographic studies of colon, biliary and urinary passages

SITE	DIAGNOSTIC FEATURES
Hepatic	See Hepatomegaly (p 1973)
Biliary	With hydrops or inflammation of the gall bladder Confirm findings with scout film for radiopaque shadows (p 1999) and cholecystography (p 2000) Painless hydrops suggests pancreatic malignancy
Renal	With ptosis or enlargement of the kidney Confirm findings by urinalysis urography and cystoscopy (p 2248)
Pancreatic	Cysts and neoplasms identified at laparotomy
Colonic	Spasm or malignancy of hepatic flexure Get barium enema (p 1890) and multiple examinations of stool for occult blood (p 3728)

in association with *mitral and tricuspid insufficiency* (p 970) *myelomalacia* (p 993) and disturbances of the *pericardium* (p 1007)

Pathology—In the early stages of hepatic congestion the *central vein* is distended with blood and the individual liver cords are more widely separated With increased engorgement the liver becomes enlarged and assumes a characteristic "nutmeg" appearance At this time the *parenchymal cells* appear altered and there is usually an increase in the *interstitial connective tissue* Quite likely these morphological changes occur as the result of tissue anoxemia The widened sinusoids rupture and deposit the brown pigment of *hemosiderosis* (p 1975)

The final anatomical expression of passive congestion is the production of a *cardiac cirrhosis* in which the atrophic parenchymal cells are replaced by connective tissue Small *adenomas* may be found scattered throughout the organ in areas where liver cells have regenerated

Hemosiderosis
Hemochromatosis (Bronze Diabetes)
Banti s Syndrome (Hepatorenal Fibrosis Congestive Splenomegaly Splenic Anemia)
Hepatolenticular Degeneration (Wilson s Disease)
Parenchymatous Degeneration
Fatty Infiltration
Hepatic Amyloidosis (Lardaceous Liver)
Glycogen Infiltration (von Gierke)
The Lipoidoses and Xanthomatoses
Infections
Catarrhal Jaundice
Liver Abscess
Hepatic Syphilis
Hepatic Amebiasis
Hepatic Distomiasis
Echinococcus Disease of the Liver

CONGENITAL MALFORMATIONS

Congenital malformations of the liver that assume clinical significance are of rare occurrence The anomalies of lobulation, blood supply and duct formation which are frequently observed during surgical procedures and at autopsy, are important to the physician only in so far as they relate to the circulation of the bile (p 1986)

MECHANICAL DISTURBANCES

THE CORSET LIVER

In the era when women affected a wasplike figure, tight lacing caused a constriction of the liver and produced a palpable irregularity of the edge the latter simulated an enlargement of the *gallbladder* It has no other clinical importance

RIEDEL S LOBE

A tonguelike lobe occasionally projects from the inferior border of the liver in the region of the gallbladder It is quite possible that this deformity is a manifestation of tight lacing The *Riedel lobe may be confused* with a *hydrops of the gallbladder* (p 2006)

HEPATOPTOSIS

Ptosis of the liver occurs as one manifestation of the *asthenic habitus* (p 3488) The lower border may be palpable at the level of the umbilicus the dome is then visible on fluoroscopy or percussed in the region of the seventh or eighth interspace in the anterior axillary line Delineation of the upper border is important in *differentiating hepatoptosis from hepatomegaly* (p 1973)

The ptosed liver usually is rotated on its long axis the superior surface is felt by abdominal palpation and the anterior face is directed toward the pelvis This circumstance makes for great difficulty in eliciting and interpreting physical signs of associated *gallbladder disease* (p 1993)

VASCULAR DISTURBANCES

HYPEREMIA OF THE LIVER BED (BILIOUSNESS)

Active congestion of the liver occurs in the gluttonous and those who habitually and consistently indulge in excessive drinking bouts Older

DIFFERENTIAL DIAGNOSIS OF

Pain in the Right Upper Quadrant

Pain in the right upper quadrant presents a perplexing diagnostic problem For complete elucidation of the problem, it may be necessary to investigate respiratory digestive biliary and urinary tracts and make examinations of urine and stool gastric and duodenal contents

SITE	DIAGNOSTIC FEATURES
Parietes	
Intercostal Neuralgia	Usually due to herpes zoster Band of hyperalgesia with later development of characteristic vesicles (p 435)
Slipping Rib	With sharply localized pain and tenderness of costochondral junction Relieved by procaine injection (p 3915)
Respiratory Tract	Lobar pneumonia pneumonitis or fibrinous *pleurisy of right base Confirm physical signs* by chest x ray
Digestive Tract	
Peptic Ulcer	History of hunger pain Free acid in gastric contents. Deformity demonstrable by barium meal (p 1780)
Cancer of Stomach	Gastric anacidity and persistent positive findings for blood in stool Filling defect in x ray following barium meal (p 1814)
Hepatic Congestion	With evidence of backward failure
Hepatitis	With jaundice May be toxic or infectious
Hypertrophic Cirrhosis	In adolescents with hepato-splenomegaly fever and clubbed fingers
Hepatic or Subphrenic Abscess	In association with appendiceal pylephlebitis or amebic dysentery Persistent fever and leukocytosis Summon surgeon for diagnostic puncture (p 3655)
Biliary	Gallbladder colic cholelithiasis cholecystitis cholangitis and choledochitis Seek evidences of jaundice Get scout film for radiopaque shadows and later prepare for cholecystography (p 2000)
Carcinoma of Hepatic Flexure	Persistent positive findings for blood in the stool (p 3728) Filling defect by barium meal or barium enema (p 1890)
Pancreatic Cyst or Neoplasm	Painless hydrops of gallbladder (Courvoisier) Consider exploratory laparotomy (p 1943)
Acute Appendicitis	With inflammation of undescended viscus
Gaseous	With distention of hepatic flexure Following intrauterine insufflation of fallopian tubes
Urinary Tract	With abscess furunculosis carbuncle or calculus of right pelvis or ureter Look for red cells and white cells in urine (p 3683) Get scout film for radiopaque shadows (p 2250) Prepare for retrograde and intravenous urogram and cystoscopy (p 2251)

Clinical Manifestations—The earliest complaint is a vague feeling of *un easiness in the right upper quadrant* This is usually accompanied by *ano rexia* resulting from engorgement of the gastric vessels Slight *tenderness* is noted in the right upper quadrant but jaundice is conspicuously absent at this time

With increase in the disturbance to the nutmeg' stage *hepatic en largement* is clearly demonstrable, in tricuspid insufficiency (p 970) the liver definitely *pulsates free fluid* begins to accumulate in the peritoneal cavity, *pretibial edema is noted a subicteric tint is present but may be* masked by cyanosis *nausea* and *vomiting* add to the patient s misery The lesion is reversible at this stage provided circulatory compensation can be reestablished

When the hepatic congestion progresses to the phase of cardiac cir rhosis the patient presents *ascites* (p 1921) and *jaundice* (p 1951) the size of the liver does not decrease with improvement in cirulatory efficiency and the prognosis is most unfavorable

The tests of *liver function* (p 1947) have only academic importance in hepatic congestion The blood bilirubin content may be slightly increased the urine frequently shows excessive amount of urobilinogen

Diagnosis—The practitioner is often confronted with the problem of dif ferentiating the gastric symptoms of *digitalis intoxication* (p 860) from those of congestion In the first instance the drug must be stopped in the latter circumstance dosage is to be continued If the pulse rate is not significantly slowed and the estimated intake of the drug seems not to have been excessive it is better to continue digitalization for an additional twenty four to forty eight hours Should the gastric symptoms persist *however the drug is then discontinued since there is nothing to gain* in proportion to the distress being inflicted on a patient already sufficiently uncomfortable Lessening of emesis despite continuance of the drug points to preexistent failure and indicates the necessity for maintaining digital ization (p 858)

Treatment—In the presence of hepatic congestion treatment is directed toward the correction of the more fundamental circulatory disturbance The patient is placed on a *bland diet* with *limitation of fluid* to 800 or 1000 cc Accessory *vitamin feedings* and parenteral injections of the sol uble components of *vitamin B complex* (p 622) protect the hepatic cells against the ravages associated with deficiency states

Phlebotomy is usually employed too little and too late The with drawal of 500 to 800 cc of blood as practiced in the gory days of the restoration period is of inestimable value particularly in the plethoric *Bloodless phlebotomy* is sometimes attempted by placing ligatures around the four extremities but it is our opinion that actual bloodletting is to be preferred

The effects of *digitalization* (p 858) are noted the *mercurial diuretics* are employed to the limit of their potentialities their efficacy may be en hanced by the preliminary oral administration of the acidifying salts such as *ammonium chloride* in doses of 3 to 6 gm daily Inhalation of high concentrations of *oxygen* (p 3827) may relieve the distress due to the heart failure and protect the liver cells from anoxemia

The enlargement of the spleen represents an attempt to take over the function of the liver as a sluice in the circulatory dynamics its removal is ill advised in conditions associated with portal hypertension (p 1960)

SUPPURATIVE PYLEPHLEBITIS

Suppurative pylephlebitis occurs as a complication of infections in areas which drain into the portal vein Thus it is observed following an acute phlegmonous or gangrenous *appendicitis* (p 1181) with ulcerative lesions of the gastro intestinal tract and with thrombosed infected hemorrhoids The lesion also may follow the injection treatment of *hemorrhoids* (p 1916)

Clinical Manifestations—The complication of suppurative pylephlebitis is suspected when a *sepsis* develops during the course of any one of the precipitating pathologic conditions The significant symptoms include increasing pyrexia chills severe abdominal pain and distention and tenderness and enlargement of the liver Jaundice does not always accompany suppurative pylephlebitis The association of a septic fever with sterile blood cultures is particularly suggestive of a pylephlebitis bacteria are filtered out in the hepatic sinusoids where they later produce multiple areas of suppuration (p 1980)

The diagnosis may be suspected from the roentgenographic demonstration of *elevation of the diaphragm* The encroachment of the liver on the thoracic cavity may collapse the right lower lobe When collaterals become established *hematemesis* and *melena* are observed from the rupture of the varices but ascites and splenomegaly rarely develop

Cryptogenic Pylephlebitis—A baffling type of pylephlebitis is encountered when the primary lesion usually a gangrenous appendicitis (p 1181) has minimal symptoms which are overlooked or not reported The patient is later observed with the fully developed syndrome of a suppurative pylephlebitis and it is only by persistent questioning that the presence of the antecedent affliction is revealed Particularly is this tragic circumstance encountered in infants and young children who cannot report subjective distress and whose vague digestive discomforts are treated by purging

Course—The course of suppurative pylephlebitis is variable Undoubtedly the lesion must occur far more often than is reported In all likelihood it is only the more advanced examples that are noted since there is a strong tendency to healing In less fortunate circumstances the sepsis continues multiple suppurative areas develop within the liver the wall of the portal vein becomes necrotic and the patient succumbs with evidences of advanced cholemia (p 1953)

Treatment—The patient with a suppurative pylephlebitis is urgently ill and requires intensive therapy using anti infective agents anticoagulants and operative surgery While these heroic therapeutic efforts are being continued the patient requires supportive treatment preferably by repeated *transfusions*

Antibiotic Therapy—Combined antibiotic therapy is required in suppurative pylephlebitis Streptomycin (p 104) and penicillin (p 106) are given by intramuscular injection or intravenous drip Heparin (p 1050) is deposited subfascially and sulfonamides may be added to the drip or they

OCCLUSION OF THE HEPATIC ARTERY

Occlusion of the hepatic artery occasionally results from operative procedures involving the biliary passages This unfortunate accident produces *anemic infarction* of the liver since the function of the portal vein as an oxygen carrier is insufficient for the enormous demands of the hepatic parenchyma Complete severance and occlusion of the hepatic artery are followed by death within a short time slower closures may be compatible with life

The clinical symptoms of acute damage to the hepatic artery include localized tenderness and rigidity fever leukocytosis anuria rapidly accumulating ascites and imminent dissolution There is no available therapeutic method of combating this condition

ANEURYSM OF THE HEPATIC ARTERY

The hepatic artery may be the site of an aneurysm as a manifestation of *subacute bacterial endocarditis* (p 1021) *periarteritis nodosa* (p 1027) or *syphilis* (p 331) The condition cannot be diagnosed during life The histories of patients who have succumbed to this disorder record attacks of pain simulating biliary colic with and without evidences of obstructive jaundice

ACUTE THROMBOSIS OF THE PORTAL VEIN

Aseptic thrombosis of the portal vein is a rare clinical condition which *is occasionally encountered in the advanced stages of the cirrhoses of the liver* (p 1069) in *polycythemia vera* (p 1092) and following *splenectomy* (p 1053) The condition is associated with a compensatory enlargement of the hepatic artery and *hemorrhagic infarcts* in the parenchyma of the liver

The patient with acute portal thrombosis is usually profoundly ill If the condition is suspected *treatment* may be conducted by heparinization using subcutaneous deposits (p 1051)

CHRONIC OCCLUSION OF THE PORTAL VEIN (CAVERNOUS TRANSFORMATION)

The portal vein may be reduced to a fibrous cord as the result of a slow thrombosis Under certain circumstances the vessel becomes *cavernomatous* Slow occlusion of the portal vein is invariably associated with *splenic enlargement* (p 1131) *ascites* (p 11) and *gastric hemorrhages* from the rupture of distended collaterals

If adequate collateral circulation is established the patient with chronic occlusion of the portal vein may survive for many years The effects of *heparinization* (p 1050) merit a therapeutic trial

PORTAL HYPERTENSION

When there is occlusion of the hepatic vessels the establishment of a *collateral circulation* is required if the patient is to survive Despite the re-routing of the blood column increased pressure develops in the splanchnic area and a portal hypertension is produced Clinically this condition is suggested by the appearance of *splenomegaly* (p 1129) dependent *edema* visibly engorged *collaterals,* bleeding from varices in the esophagus or stomach and an increased tendency to the production of *hemorrhoids* (p 1016)

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may be given orally (p 88) Antibiotics in the drip may be interspersed with infusions of saline dextrose plasma or blood

Surgery—Surgical attempts to ligate the ileocolic vein should be deferred until the effects of non operative therapy have been noted If hepatic abscesses develop they require incision and drainage whether or not chemotherapy has proved successful

NEOPLASMS

BENIGN TUMORS OF THE LIVER

Congenital cysts hemangiomas and *adenomas* of the liver are discovered at autopsy with some frequency they rarely give rise to symptoms and the finding is usually accidental The congenital cysts of the liver occur in association with *polycystic disease of the kidneys* (p 2291) The presenting symptoms are always due to the nephropathy Hemangiomas occasionally produce a *venous bruit* in the hepatic region

A benign neoplasm of tremendous size may produce an obstructive type of jaundice (p 1953) by pressure on the duct system The abdomen is then explored with the strong suspicion that a malignant lesion will be encountered If the benign character of the lesion is recognized the surgeon may be able to relieve the pressure and dissipate the icterus by removal of the growth

PRIMARY CARCINOMA OF THE LIVER

Primary carcinomas of the liver may be solitary or multiple they may arise in the duct system or in parenchymal tissue they are very rarely observed except in association with the chronic irritation of *hepatic distomiasis* (p 1982) As further evidence of the relationship between chronic irritation and malignancy liver neoplasms occasionally become implanted upon a *cirrhosis* (p 1969) or a *hemochromatosis* (p 1976) The associated *avitaminoses* (p 616) may be of accessory importance

The diagnosis of primary carcinoma of the liver requires surgical exploration or autopsy The patient notes loss of weight weakness jaundice a tendency to repeated internal hemorrhages abdominal pain and unexplained fever The liver is enlarged and there may be an associated splenomegaly (p 1129) ascites develops in the terminal stages

There are no methods of *treatment* other than to make the patient comfortable

PRIMARY SARCOMA OF THE LIVER

Primary hepatic sarcoma is a medical curiosity resembling carcinoma until sections are studied histologically

METASTATIC CARCINOMATOSIS OF THE LIVER

Metastatic carcinomatosis of the liver occurs with g eat frequency The metastases may be multiple or single the *primary growth* may be intra abdominal or in a distant structure such as the breast the lung or the brain The primary focus may be small and completely silent it may have been eradicated previously by a curative operation or it may be quite obvious

The *clinical manifestations* of hepatic carcinomatosis are late in their development and most insidious The liver may reach a gigantic size there may be almost complete replacement of parenchymal cells by the lawless invaders while the patient has no complaint other than fatigability anorexia and a sense of pressure in the upper abdomen *Weight loss* may be obscured by the development of an ascites The *spleen* rarely enlarges unless the vein becomes thrombosed The occurrence of *jaundice* (p 1951) is variable and depends wholly upon the chance factor of mechanical obstruction As evidence of the function of the liver in heat regulation hepatic carcinomatosis is usually associated with an *aseptic fever* (p 23) The terminal manifestations are progressive wasting cachexia and cholemia

Symptomatic treatment is limited to *paracentesis abdominalis* (p 1990) Often the removal of ascitic fluid is followed by apparent increase in the rate of dissolution

METABOLIC DISTURBANCES

TOXIC HEPATITIS

Toxic hepatitis may be produced by a variety of chemical metabolic or infectious agents In each instance there is damage to the liver parenchyma with the production of a *hepatic jaundice* (p 1959) The clinical picture is often confused by the addition of features of *obstructive* or *hemolytic jaundice* when the hepatitis becomes complicated by inflammatory obstruction of the small bile ducts and evidences of blood destruction

Etiology—The commoner causes of hepatocellular jaundice are exogenous drugs and chemicals the endogenous products of metabolism and the toxins of infection

Exogenous Chemicals—The chemical and pharmacological substances which most frequently cause toxic hepatitis are cinchophen chloroform carbon tetrachloride phosphorus the arsenicals and the sulfonamides Less frequently the disturbance is produced by trinitrotoluol phenylhydrazine tetrachlorethylene paraphenylendiamine alcohol bismuth snake venom liver extract tannic acid and the toxins of mushroom poisoning (p 240)

CINCHOPHEN—Cinchophen (p 3832) hepatitis is a puzzling clinical condition The drug is taken with impunity by thousands of patients for the relief of *arthralgias* (p 2802) and *gout* (p 2867) Nevertheless in isolated instances under circumstances that are not understood and cannot be anticipated a fulminating and fatal type of liver damage may be produced

CHLOROFORM—Chloroform (p 3924) poisoning is infrequently observed since the introduction of the newer anesthetic agents (p 4009) The manifestations of the intoxication may be immediate or delayed The symptoms include intractable vomiting with multiple bleedings jaundice may be relatively inconspicuous Death may occur after several days autopsy reveals extensive hepatic necrosis with rupture of bile capillaries

CARBON TETRACHLORIDE—Carbon tetrachloride (p 1897) is used in industry as a chemical solvent and in therapeutics for the treatment of *helminthiasis* (p 1893) It may produce a toxic hepatitis with nephritis within twelve hours after exposure Often the untoward manifestations seem to be precipitated by an associated alcoholic spree The patient may

rapidly succumb completely recover or develop a complicating cirrhosis of the liver (p 1969)

PHOSPHORUS —Hepatitis due to phosphorus (p 729) is less rarely en countered than in previous decades when the substance was taken with suicidal intent or as an *abortifacient* The toxic manifestations include the sudden appearance of jaundice abdominal pain and multiple hemorrhages

ARSENIC —Arsenical hepatitis is more likely to follow the use of triv alent preparations such as *carbarsone* (p 530) Of the pentavalent ar senicals *arsphenamine* is most hepatotoxic, *mapharsen* and *tryparsamide* are least likely to cause liver damage

The *pathogenesis* of arsenical jaundice has been considerably debated In some instances the liver damage may be caused by the syphilitic in fection rather than the therapeutic endeavor The infrequent occurrence of the condition in the intensive treatment of syphilis (p 344) argues against the factor of overdosage idiosyncrasy and intercurrent infection seem to be more likely precipitants

The *symptoms* of arsenical hepatitis may be early and acute they may be delayed and insidious In either event the complication is of seri ous import and may terminate fatally Should recovery be experienced the arsenical drugs are not to be administered again Often the hepatitis is associated with other manifestations of toxicity

SULFONAMIDES —As with other substances capable of great good the *sulfonamides* may produce toxicologic phenomena including hepatitis This unfortunate complication usually occurs a week or more after therapy has been begun and is often associated with a *toxicoderma* (p 94) While the majority of patients recover others progress to acute yellow atrophy and death a small number are left with a cirrhosis

MISCELLANEOUS —Toxic hepatitis from the remaining exogenous chem ical is rarely observed Liver damage may be caused by *dinitrophenol* used in the treatment of obesity (p 696) *phenylhydrazine* employed in the management of polycythemia vera (p 1092) poisoning with *Amanita phalloides* the toxic *mushroom* (p 240) *inorganic arsenicals* such as Fow ler s solution (Liquor Potassii Arsenitis) or *insecticides trinitrotoluol* (T N T) used in munitions manufacture *paraphenylendiamine* contained in hair dyes *snake venom liver extract bismuth* the abuse of *alcohol* and overzealous use of *tannic acid* in the treatment of burns (p 3981)

Endogenous Metabolic Products—Toxic hepatitis may be experienced in the course of a *hyperthyroidism* in the pernicious vomiting of *preg nancy* and in *eclampsia*

HYPERTHYROIDISM —The excessive metabolic demands in hyperthy roidism (p 1197) may produce varying degrees of hepatic damage The liver glycogen is diminished the protein reserve is drawn upon for its carbohydrate fraction protective vitamins may not be sufficiently stored and the parenchymal cells reflect morphologically the ravages of the dis ease Despite the severity of the insult to the liver clinical jaundice and evidences of dysfunction are rarely observed other than in the *thyrotoxic crises* (p 1207) Under other circumstances the appearance of jaundice in hyperthyroidism suggests the more likely presence of some obstructive phenomenon relative to the gall sac or the biliary passages (p 1953)

PERNICIOUS VOMITING OF PREGNANCY AND ECLAMPSIA —Normal preg

nancy produces no disturbance in liver function In *pernicious vomiting of pregnancy* (p 2637) toxic hepatitis and acute yellow atrophy may complicate the pre-existent metabolic disturbance Hepatic lesions are also strikingly apparent in *eclampsia* (p 2638) when areas of hemorrhagic necrosis are seen in the parenchymal cells and fibrin thrombi are present in the radicles of the portal vein Current opinion favors the view that the liver disturbance is a result rather than a cause of the disturbances of pregnancy The use of the potentially hepatotoxic chloroform in obstetrical anesthesia cannot be too vigorously condemned

Infection—Toxic hepatitis of infectious origin may result from inflammatory processes involving the biliary passages or it may be associated with generalized systemic invasion

BILIARY INFECTIONS—Toxic hepatitis accompanies biliary infections in *catarrhal jaundice* (p 1975) *cholangitis* (p 2010) *suppurative pylephlebitis* (p 1961) and *liver abscess* (p 1980)

GENERAL INFECTIONS—Toxic hepatitis is a prominent feature in the viral infection of *yellow fever* (p 477) and the spirochetal invasion of *Weil s disease* (p 360) it occurs also in syphilis (p 331) lobar pneumonia (p 2171) infectious mononucleosis (p 466) and the bacteremias

While hepatitis and jaundice are intrinsic portions of the clinical manifestations of yellow fever and Weil s disease the problem of icterus in *syphilis* is much more complicated The icterus may result from *acute interstitial hepatitis* of congenital syphilis (p 2787) or secondary syphilis (*icterus syphiliticus praecox*) it accompanies a syphilitic cirrhosis and pressure from a hepatic gumma it may be produced by chemotherapy with arsenic (p 1964) or bismuth

The syphilitic like the normal individual may develop *catarrhal jaundice* (p 1979) as an incidental and unrelated circumstance The problem of jaundice in syphilis is made increasingly difficult by the fact that a serologically negative individual who develops a catarrhal jaundice or an infectious mononucleosis often develops false positive serologic tests (p 337) The conscientious practitioner must be particularly alert to the last circumstance lest the patient be unjustly stigmatized and unnecessarily treated

Pathology—In toxic hepatitis the liver parenchyma reveals focal areas of necrosis the individual cells show fatty degeneration cloudy swelling or actual necrosis inflammatory changes are present in the connective tissue between the lobules the canaliculi contain desquamated material and bile thrombi The liver is grossly enlarged due to swelling of the cells and edema of vascular origin the consistency is softer than normal there is often an associated process of similar character in the kidneys and pancreas

Toxic hepatitis may terminate in complete healing it may progress to *acute* or *subacute atrophy* (p 968) in certain instances the final outcome is the production of a *cirrhosis* (p 1969)

Pathologic Physiology—The pathologic physiology of toxic hepatitis is not as simple as the nomenclature would indicate since three factors are operative to a greater or less degree in addition to the *hepatic cellular insufficiency* there is *inflammatory obstruction* of the bile canaliculi and a certain amount of *blood destruction* As a result the analysis of the jaundice reveals *prehepatic hepatic* and *posthepatic elements* (p 1952) The last simulating true obstruction results from a back diffusion or regurgitation of bile into the blood when necrosis and edema interrupt

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PERNICIOUS VOMITING OF PREGNANCY AND ECLAMPSIA —Normal preg

Treatment —The treatment of toxic hepatitis is far from satisfactory *Pregnancies* (p 2649) are best terminated *hyperthyroidism* (p 1197) is treated with iodide and the indicated surgical procedures but even when the hepatotoxin can be identified and eliminated the course of the disease may be progressively downhill Antidotal therapy is disappointing injections of *sodium thiosulfate* accomplish nothing in our experience a crude liver extract (intraheptol) may be cautiously injected intravenously each day starting with 1 cc in 25 cc saline and increasing to 10 cc in 50 cc of diluent

Diet —Dietotherapy is of important significance in the patient whose stomach is tolerant An attempt is made to provide 300 to 500 gm of *carbohydrate* as a daily quota with a minimum of 100 gm of *protein* and as little fat as is possible alcoholic drinks are forbidden

CARBOHYDRATE —To accomplish the rich carbohydrate feedings the patient is tempted with sweet potatoes fresh fruit with added sugar or lactose fruit juice dried or stewed fruits bread cereals dates rice macaroni spaghetti cake with icing waffles or hot cakes with maple syrup or honey jam sugar marshmallows candy syrup ice cream sodas maple syrup cornstarch rice and tapioca puddings ripe bananas and in between feedings of hard candies and lollypops

PROTEIN —The protein in our opinion may be given in the form of meat fish poultry or shellfish according to the individual taste condiments and spices are best avoided

FLUID —Sufficient fluid should be given to the hepatotoxic patient to obtain a daily urinary output of at least 1500 cc The use of broth tea coffee and plain water is advised carbonated drinks take up too much space for the accomplishment of a satisfactory carbohydrate intake

PARENTERAL FEEDINGS —Parenteral feeding is required for patients with intolerance of the stomach and those who fail to ingest sufficient quantities of carbohydrate and fluid With a negligible gastric intake we favor a *continuous intravenous drip* (p 3775) of 5 per cent dextrose in saline To this are added the available soluble vitamins plasma amino acid or whole blood according to indication With a tendency to edema saline is omitted from the infusate and the dextrose is given in distilled water

When the parenteral feeding is supplementary to a slightly inadequate dietary intake the patient may be given several daily intravenous injections of a concentrated sugar solution such as 25 to 50 cc of 25 or 50 per cent *dextrose* or *sucrose*

Insulin —Unless the patient develops glycosuria as the result of the heavy carbohydrate ration we do not favor injections of *insulin* Many clinicians of wide experience do however use insulin as part of the routine of therapy injecting 5 to 15 units before or with each principal feeding

The Bowels —It is our practice to care for the bowels by a simple *enema* or a *colon irrigation* We are opposed to *calomel purging* we do not favor the daily use of *salines* since they tend to further deplete and dehydrate the patient

Transduodenal Lavages and Feedings —Despite the enthusiasm of proponents we do not favor transduodenal lavages or feedings Most patients are sufficiently uncomfortable from their disease without the addition of rubber spaghetti to augment their difficulties

the continuity of the finer biliary radicles and intrabiliary pressure is elevated

Clinical Manifestations—The onset of toxic hepatitis is usually preceded by *indeterminate prodromes* which include malaise anorexia generalized myalgia nausea vomiting and a slight elevation of temperature The breath may have a hepatic amine odor there may be some upper abdominal discomfort with tenderness over the liver bed

The nature of the affliction does not become apparent until the appearance of the *jaundice* This may be observed first as a *subicteric tinge* to the cornea it may be noted that the *urine* has become dark and the *stools* are of a light coloration At this time the temperature rises higher anorexia is complete nausea and vomiting are constant the liver becomes palpably enlarged and the tip of the spleen may be felt *Bradycardia* and *pruritus* precede and postdate the jaundice which deepens but does not assume the deep olive hue of the obstructive variety The presence of *ascites* (p 1921) has ominous prognostic significance suggesting transition to the stage of acute yellow atrophy

Laboratory Data—Examinations of the urine stool and blood provide information of diagnostic and prognostic value

Stools—The stools are light in color but they are not *acholic* (p 3729) *occult blood* is frequently present probably as the result of small gastro intestinal erosions or through seeping of blood secondary to diminution in the contents of vitamins C and K

Urine—The urine is highly concentrated and deeply stained *bile pigments* are demonstrable *tyrosine* and *leucine* crystals are absent the *albuminuria* is no more than a trace unless there is the ominous *hepato renal syndrome* (p 1968)

Blood—The bilirubin content of the *blood serum* is increased the *icterus index* is elevated the *van den Bergh tests* are directly positive depending upon the amount of regurgitant bile pigment in the blood serum the *cholesterol* level is depressed with extreme liver damage the *ester fraction* may drop to zero Elevations of cholesterol and ester fractions constitute optimistic prognostic signs

The more complicated *tests of liver function* are often confusing and may suggest both hemolytic and obstructive factors the level of *plasma prothrombin* falls below 80 per cent with significant hepatic insufficiency the intramuscular injection of 2 cc of *menadione* (p 630) corrects the defect if the hepatic cells are capable of response

Laboratory data may add confusion to the clinical problem by the appearance of a false positive serologic test for *syphilis* (p 337)

Course—In favorable instances jaundice persists for one to two months and then begins to fade as the patient initiates *convalescence* Complete recovery may take three months or more at the end of which time the patient is restored to pristine health so far as can be determined

Under less favorable conditions the icterus persists and the stages of *acute* or *subacute yellow atrophy* (p 1968) are entered with a fatal termination in an appreciable number of patients The transition to *cirrhosis* (p 1969) is rarely demonstrable since the consequences may not become apparent for decades after the original insult

Diagnosis—See *Jaundice* (p 1951)

Treatment—The treatment of toxic hepatitis is far from satisfactory *Pregnancies* (p 2649) are best terminated *hyperthyroidism* (p 1197) i treated with iodide and the indicated surgical procedures but even when the hepatotoxin can be identified and eliminated the course of the dis ease may be progressively downhill Antidotal therapy is disappointing injections of *sodium thiosulfate* accomplish nothing in our experience a crude liver extract (intrahepto!) may be cautiously injected intra venously each day starting with 1 cc in 25 cc saline and increasing to 10 cc in 50 cc of diluent

Diet—Dietotherapy is of important significance in the patient whose stomach is tolerant An attempt is made to provide 300 to 500 gm of *carbohydrate* as a daily quota with a minimum of 100 gm of *protein* and as little fat as is possible alcoholic drinks are forbidden

CARBOHYDRATE—To accomplish the rich carbohydrate feedings the pa tient is tempted with sweet potatoes fresh fruit with added sugar or lac tose fruit juice dried or stewed fruits bread cereals dates rice maca roni spaghetti cake with icing waffles or hot cakes with maple syrup or honey jam sugar marshmallows candy syrup ice-cream sodas maple syrup cornstarch rice and tapioca puddings ripe bananas and in between feedings of hard candies and lollypops

PROTEIN—The protein in our opinion may be given in the form of meat fish poultry or shellfish according to the individual taste condi ments and spices are best avoided

FLUID—Sufficient fluid should be given to the hepatotoxic patient to obtain a daily urinary output of at least 1500 cc The use of broth tea coffee and plain water is advised carbonated drinks take up too much space for the accomplishment of a satisfactory carbohydrate intake

PARENTERAL FEEDINGS—Parenteral feeding is required for patients with intolerance of the stomach and those who fail to ingest sufficient quanti ties of carbohydrate and fluid With a negligible gastric intake we favor a *continuous intravenous drip* (p 3775) of 5 per cent dextrose in saline To this are added the available soluble vitamins plasma amino acid or whole blood according to indication With a tendency to edema saline is omitted from the infusate and the dextrose is given in distilled water

When the parenteral feeding is supplementary to a slightly inadequate dietary intake the patient may be given several daily intravenous injec tions of a concentrated sugar solution such as 25 to 50 cc of 25 or 50 per cent *dextrose* or *sucrose*

Insulin—Unless the patient develops glycosuria as the result of the heavy carbohydrate ration we do not favor injections of *insulin* Many clinicians of wide experience do however use insulin as part of the rou tine of therapy injecting 5 to 15 units before or with each principal feeding

The Bowels—It is our practice to care for the bowels by a simple *enema* or a *colon irrigation* We are opposed to *calomel purging* we do not favor the daily use of *salines* since they tend to further deplete and de hydrate the patient

Transduodenal Lavages and Feedings—Despite the enthusiasm of pro ponents we do not favor transduodenal lavages or feedings Most patients are sufficiently uncomfortable from their disease without the addition of "rubber spaghetti" to augment their difficulties

the continuity of the finer biliary radicles and intrabiliary pressure is elevated

Clinical Manifestations—The onset of toxic hepatitis is usually preceded by *indeterminate prodromes* which include malaise anorexia generalized myalgia nausea vomiting and a slight elevation of temperature The breath may have a hepatic amine odor there may be some upper abdominal discomfort with tenderness over the liver bed

The nature of the affliction does not become apparent until the appearance of the *jaundice* This may be observed first as a *subicteric tinge* to the cornea it may be noted that the *urine* has become dark and the *stools* are of a light coloration At this time the temperature rises higher anorexia is complete nausea and vomiting are constant the liver becomes palpably enlarged and the tip of the spleen may be felt *Bradycardia* and *pruritus* precede and postdate the jaundice which deepens but does not assume the deep olive hue of the obstructive variety The presence of *ascites* (p 1921) has ominous prognostic significance suggesting transition to the stage of acute yellow atrophy

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Diagnosis—See *Jaundice* (p 1951)

ance are due partially to a *hypoproteinemia* (p 706) resulting from the inability of the liver to produce serum albumin Further evidence of the extent of the hepatic damage is attested by the presence of an *aseptic fever* (p 23) and of leucine and tyrosine crystals in the urine

With the onset of acute yellow atrophy other abnormal laboratory findings include *secondary anemia* increase in the *sedimentation rate* decrease in the *prothrombin level* failure of response to *vitamin K* elevation of the *nonprotein nitrogen of the blood* decrease in *blood urea* and *blood sugar* increase of *blood bilirubin* a direct positive *van den Bergh test* fall of *cholesterol* and its *ester fraction* to the vanishing point and a greater tendency to develop confusing *serologic tests* for *syphilis*

The *stool* shows varying amounts of *urobilin* which disappears as the liver damage becomes more severe The urinary content of *bilirubin* decreases in amount as the clinical course becomes more grave

Diagnosis —See *Jaundice* (p 1951)

Prognosis —The prognosis in acute yellow atrophy is most unfavorable complete recoveries may be experienced more frequently those who survive develop a cirrhosis

Treatment —The treatment of acute yellow atrophy of the liver is similar to that employed in the management of a hepatitis (p 1967) Greater reliance is placed upon intravenous medication since gastric intolerance makes it impossible to carry out the dietetic program

With the development of ascites (p 1921) there is a great temptation to perform paracentesis abdominalis (p 1920) This procedure is best postponed as long as is compatible with the patient s comfort since the tap is often followed by the rapid onset of *cholemia* (p 1953)

SUBACUTE RED ATROPHY

The patient who survives an acute yellow atrophy for more than a month may be assumed to have progressed to the subacute stage of red atrophy

Subacute atrophy may involve only portions of the liver the intervening hepatic tissue remains normal and may undergo a hyperplastic change with nodule formation Partial recovery is possible when the area of compensatory hyperplasia functions for the organ as a whole *Treatment* is conducted as in toxic hepatitis (p 1967)

PORTAL CIRRHOSIS (ATROPHIC LAËNNEC ALCOHOLIC HOBNAIL OR GIN DRINKER S CIRRHOSIS)

Hepatic cirrhosis of portal distribution becomes a less mysterious affliction when it is regarded as a fibrosis that follows upon acute or chronic inflammation of the liver cells In contradistinction to biliary cirrhosis next to be described (p 1972) the pathological evidence suggests that the toxic process involves the *parenchymal tissue* of the liver rather than the excretory mechanism by which bile is conveyed into the intestine

Etiology —According to older concepts portal cirrhosis was a consequence of *chronic alcoholism* The more modern view attributes the disturbance to any of the *hepatotoxic agencies* (p 1963) and regards the lesion in drunkards as a manifestation of *avitaminosis* rather than poisoning resulting from tippling See Fig *2H* (p 9)

Drug Therapy—The patient with toxic hepatitis should receive a minimum amount of drug therapy It is unwise to further burden the liver with the necessary detoxification of most pharmacological agencies the incomplete inactivation of preparations such as the *opiates* may cause profound effects when hepatic function is damaged

Bile Salts and Vitamin K—Administrations of bile salts (p 1990) with vitamin K are especially advocated in patients who show evidences of a hemorrhagic tendency The vitamin may be given orally as menadione (p 630) in doses of 5 to 10 mg for parenteral administration a daily amount of 2 mg is sufficient The *bile salts* are given as the salts of the oxidized bile acids and the synthetic dehydrocholic acid in amounts of 0 3 to 0 6 gm (5 to 10 grains) Natural bile salts and extracts of ox bile also may be used for intravenous injection sodium dehydrocholate is given in amounts of 3 to 10 cc of a 20 per cent solution

Antipruritics—Often the presenting complaint of the patient is the intractable itch An attempt is made to control this symptom by external measures such as hot baths containing bicarbonate of soda bran or epsom salts A calomine and zinc lotion may be applied to localized areas if this is unsuccessful the preparation is fortified with 0.5 per cent menthol and/or 0 25 per cent phenol Pyribenzamine (p 565) is given orally

If no relief is obtained from external measures *ergotamine tartrate* (p 3883) is prescribed using 1 0 mg four times daily by mouth or the subcutaneous injection of 0 5 to 1 0 mg before retiring Relief may also be afforded by intramuscular injections of *calcium gluconate* (p 604)

ACUTE YELLOW ATROPHY

Acute yellow atrophy of the liver is an advanced stage of toxic hepatitis

Pathology—In acute yellow atrophy of the liver the hepatitis progresses to massive necrosis and autolysis of the parenchyma In the first and second weeks of the process the organ appears yellow as the result of the necrotic disturbance With further progression and resorption of the autolyzed cells the remaining vascular tissue produces a red coloration as the organ shrinks and becomes flaccid

The distinction between acute yellow atrophy and *subacute red atrophy* is essentially one of degree Up to the end of the first month of the disturbance the lesion is that of acute yellow atrophy after this time it is more correct to speak of a subacute red atrophy Characteristic of both stages is the lack of the reaction on the part of the connective tissue

Clinical Manifestations—The transition of hepatitis to acute yellow atrophy is suspected when the *jaundice* deepens There is continuance of the vomiting *muscle fibrillations* are observed *liver dulness* becomes lessened and may be wholly obliterated evidences of the hemorrhagic diathesis are present purpuric lesions are seen the patient becomes *comatose* but may have *convulsions* *ascites* collects severe *pain* may be experienced in the epigastrium or the right upper quadrant Despite the continuance of the ominous course the jaundice may appear to lighten this paradox has been explained by failure of the reticulo endothelial cells to metabolize the bilirubin excreted by the parenchymal cells

Laboratory Data—With the development of ascites the urine volume falls and there may be *anuria* with *edema* The disturbances in water bal

type of *anemia* occasionally the hemogram is of the *hyperchromic variety* (p 1077) when the liver is no longer capable of producing an adequate supply of the erythrocyte maturation factor (p 1038) Additional blood findings include *hypoproteinemia* (p 706) a reversal of the *albumin globulin ratio* (p 5) and a *hyperbilirubinemia* (p 1951)

The urine contains increased amounts of *urobilin* and *urobilinogen* (p 3686) When jaundice occurs *bilirubin* and *albumin* are also noted in the voided specimen The stools are normal in appearance until the terminal stages when they may become *acholic* gross and occult *blood* are often present due to oozing from hemorrhoids or the internal congestion of portal hypertension (p 1960)

Of the more complicated laboratory tests the *van den Bergh* is positive by the indirect methd the *cholesterol and ester* figures are low the *phosphatase* reaction is normal the *galactose* mechanism is unimpaired but the *cephalin cholesterol flocculation test* indicates liver damage (p 1947)

Diagnosis —See *Jaundice* (p 1951) *Biliary Cirrhosis* (p 1972)

Prognosis —Before the pathogenesis of portal cirrhosis was more clearly understood the disease generally terminated fatally within three years of the development of the ascites Current methods of therapy have altered this gloomy outlook an amazing degree of well being may be established and maintained with proper cooperation

Treatment —The treatment of portal cirrhosis requires an intense effort on the part of the practitioner and complete cooperation by patient and family with particular reference to prophylaxis

Diet —Dietotherapy is of the greatest value *sugars* and *starches* are given to the extent of 300 to 500 gm daily the *protein intake* is maintained in the neighborhood of 100 gm chiefly of vegetable origin or derived from milk or egg white

Vitamins —Large doses of *vitamins* are given orally and parenterally *oleum percomorphum* (2 cc daily) supplies A and D *liver extract* is injected intramuscularly using 2 cc doses three times a week *thiamine chloride niacin* and *riboflavin* are given intravenously three or four tablets of *brewers yeast* are swallowed at the end of each meal if less than 300 cc of orange juice are drunk 50 to 100 mg of *ascorbic acid* are prescribed by mouth or parenterally If there is any tendency to bleed *vitamin K* (p 630) is included in the program using *menadione* 10 to 25 mg daily Intravenous injections of intraheptol (p 1967) merit trial

Restoration of Blood Protein —The patient with ascites and anasarca may be assumed to have a hypoproteinemia (p 706) To the other measures must then be added *intravenous infusions* of amino acids plasma or whole blood Choline and cysteine given orally in 2 0 gm doses have lipotropic activity and may be of value when fatty infiltration is present

Diuresis —In the attempt to conserve body protein the *mercurial diuretics* are administered for the purpose of shifting the ascitic fluid In the early stages the use of the drug may be followed by a tremendous outpouring of urine with a loss of 5 to 10 pounds in body weight the abdominal circumference visibly lessens and all evidences of free intra abdominal fluid may be dissipated by repeated injections

Pathology—*In the early stages of a portal cirrhosis the liver is temporarily enlarged* due to preliminary fat infiltration As the process continues atrophy of the liver cells and contraction of the *scar tissue result in shrinkage of the organ* which becomes hard and gritty The surface appears granular with elevations or hobnails caused by islands of hyperplastic liver tissue The architecture of the *organ is completely irregular and chaotic areas of* greenish yellow or yellowish brown parenchyma being separated by bands of grayish white fibrous tissue

Microscopic sections reveal distortion and atrophy of the liver lobules the hepatic veins occupy eccentric positions bile ducts may be collapsed or distended the individual liver cells may show parenchymatous hyaline fatty or pigmentary changes the stroma is con spicuously increased through the appearance of broad bands which separate islands of liver cells from arteries veins and bile capillaries

Clinical Manifestations—Portal cirrhosis may remain *compensated* for a long period of time Sooner or later the asymptomatic phase is fol lowed by manifestations due to congestion avitaminosis and hepatic insuf ficiency

The Congestive Phase—The early symptoms of portal cirrhosis are due to vascular congestion of the digestive organs The patient notes vague gastro intestinal distress anorexia nausea vomiting diarrhea flatulence *bad breath coated tongue and what is commonly described as* bilious ness Symptoms are worse in the morning when the patient wakens with headache *the alcoholic immediately gulps down a hair of the dog that* bit him '

On rare occasions the congestive phase is initiated by an episode of bleeding there may be severe *epistaxis* (p 2123) *hematemesis* or *melena* (p 1843)

Avitaminoses—The general distaste for food particularly in alcoholics results in the intake of a deficiency diet and resultant loss of weight The indigent drunkard who spends his money on liquor has nothing left with which to purchase nutriment He is more likely to be afflicted with cir rhosis than the affluent drunk who has money left over for tempting victuals

The superimposed avitaminosis adds a galaxy of symptoms to those due to congestion lack of *B complex* results in fatigability a peripheral *neuritis (p 1499) cardiac edema (p 711) glossitis (p 1707) and stomatitis* (p 434) night blindness and dryness of the skin are due to *deficiency of* A the tendency toward *bleeding may be partially mechanical but* attests to an impoverishment of *C and K*

Hepatic Insufficiency—After a variable period the stage of *insufficiency* is reached Early symptoms are intensified *ascitic fluid* accumulates in the peritoneal cavity the body shrinks while the belly swells *hemorrhoids* protrude *jaundice* appears attacks of pain in the right upper quadrant simulate *biliary colic pruritus* adds to general discomfort there is a cer tain amount of *mental deterioration* and alcoholics develop the *psychoses* elsewhere described (p 1384)

Beside the jaundice and ascites physical examination reveals atrophy of the liver with some enlargement of the *spleen* the skin is sallow and covered with *angiomas telangiectases* and *scratch marks* there may be an *acne rosacea* the collateral superficial abdominal veins are distended and tortuous forming the caput medusae

Laboratory Data—Most patients with cirrhosis develo secondary

type of *anemia* occasionally the hemogram is of the *hyperchromic variety* (p 1077) when the liver is no longer capable of producing an adequate supply of the erythrocyte maturation factor (p 1038) Additional blood findings include *hypoproteinemia* (p 706) a reversal of the *albumin globulin ratio* (p 5) and a *hyperbilirubinemia* (p 1951)

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When the discomfort of the patient requires the mechanical removal of the ascitic fluid an attempt is made to *prevent reaccumulation* by spaced injections of the mercurial diuretics The body weight is used as a guide and the intervals may be two days to two weeks The effects are enhanced by the oral administration of the *acidifying salts* 3 to 6 gm of *ammonium chloride* are given daily in divided doses for two or three days on and two or three days off

Paracentesis Abdominis —If a sustained effort to avoid paracentesis abdominis fails there is no alternative but to perform an abdominal tap Reaccumulation of fluid may be prevented or delayed by the use of the diuretics (p 2257)

Surgery —With a progressively unfavorable course or uncontrollable bleeding surgical efforts at the control of a portal cirrhosis have been attempted by *splenectomy* the *injection of esophageal varices* through the esophagoscope or by *ligation of the coronary veins of the stomach* Such heroic measures are more to be commended for their daring than their therapeutic potentialities

Surgeons have attempted to aid in the collateral circulation by performance of *omentopexy* (Talma operation) The results as might be anticipated have been almost uniformly unsatisfactory

Prophylaxis —In those fortunate instances in which compensation is restored the patient is warned that recurrences are certain to be experienced upon exposure to hepatotoxins particularly indulgence in alcohol to the exclusion of a balanced diet With regard to liquor as elsewhere discussed (p 3851) we oppose tapering off and insist upon complete abstinence preferably with institutional care

In his dealings with those who have recovered from a portal cirrhosis the practitioner avoids the use of potentially toxic drugs these include arsenicals anesthetics anthelmintics opiates barbiturates and the sulfonamides

BILIARY CIRRHOSIS (HANOT OBSTRUCTIVE OR HYPERTROPHIC CIRRHOSIS

Biliary cirrhosis is much less frequently observed than the portal variety The distribution of the fibrosis about the smaller biliary ducts suggests that the prime cause rests in some inflammatory disturbance of the collecting and excretory systems

Etiology —Since biliary cirrhosis is seen most often in *young people* it is suggested that the disturbance results from episodes of *catarrhal jaundice* (p 1979) *cholangitis* or *pericholangitis* The gallbladder seems not to participate in the process

Pathology —In a biliary cirrhosis the liver is enormously enlarged the dark green surface is finely granular the spleen is enlarged and firm

Microscopic examination shows that the main proliferation of the stroma has occurred about the radicles of the bile ducts The involvement is principally *pericholangitic* with little scarring in the region of the portal vein The architecture of the liver is less disturbed than in a portal cirrhosis there is less involvement of the parenchymal cells The splenic sinuses appear distended and the pulp is markedly proliferated

Clinical Manifestations —The patient with biliary cirrhosis often gives a history of a pre existent *respiratory infection* or of repeated attacks of *abdominal* pain associated with fever These prodromal signs suggest that

the hepatic disturbance may be secondary through hematogenous lym phogenous or direct extension

DIFFERENTIAL DIAGNOSIS OF

Enlargement of the Liver (Hepatomegaly)

Because of the multiplicity of its functions enlargements of the liver may be due to many causes In the end differential diagnosis is often based solely on the clinical findings since laboratory tests have not been perfected to the point where the practitioner may place une quivocal reliance upon them

	DIAGNOSTIC FEATURES
Mechanical	Ptosis or Riedl s lobe without associated dis turbances in function
Hematopoietic	Anemias leukemias Hodgkin s disease and the lipoidoses Check hemogram (p 3704) and sternal marrow if necessary (p 1043) Note associated splenomegaly and generalized lymphadenopathy
Circulatory	In backward failure With pulsation in tri cuspid insufficiency In suppurative pyle phlebitis especially after appendicitis
Metabolic	With cloudy swelling amyloidosis fatty and glycogen infiltrations hemosiderosis lipoidoses and hemochromatosis Look for splenomegaly and lymphadenopathy in the lipoidoses Note glycosuria and iron pigment of skin in hemo chromatosis
Neoplastic	Primary and metastatic malignancy Consider laparotomy
Inflammations and Infections	
Atrophic Cirrhosis	With later diminution in size of liver evidences of portal congestion and ascites Often associ ated with alcoholism
Biliary Cirrhosis	In younger individuals with fever spleno- megaly early jaundice and periods of exacer bation and remission
Infectious Hepatitis	Acute episodes of catarrhal jaundice Associ ated with fever and gastro intestinal disturb ances followed by recovery
Liver Abscess	Solitary or multiple former often of amebic origin with amebae obtained in stool or by liver puncture (p 523) Multiple abscesses usually secondary to suppuration in biliary passages or appendicitis with pylephlebitis Try therapeutic tests with emetine in amebic abscess (p 529) and with anti infective agents in multiple abscesses (p 1980)
Neonatal Syphilis	With positive serology in maternal umbilical or fetal blood.
Hydatid Disease	Echinococcus infestation with eosinophilia palpable thrill to tumor and hooklets recovered by aspiration.
Hepatic Distomiasis	Liver fluke with ova demonstrable in stools or by puncture (p 1982)

The first symptom directly referable to the local condition is the protrusion of the abdomen caused by the *hepatosplenomegaly* (p 1129) *jaundice* (p 1951) is soon noted and its tint is olive green in contrast to the orange hue of a toxic hepatitis (p 1965) Biliary cirrhosis most often occurs in *young males* there is no history of antecedent alcoholism or exposure to hepatotoxic substances Ascites rarely develops *splenic enlargement* is invariable *clubbing of the fingers* is commonly encountered

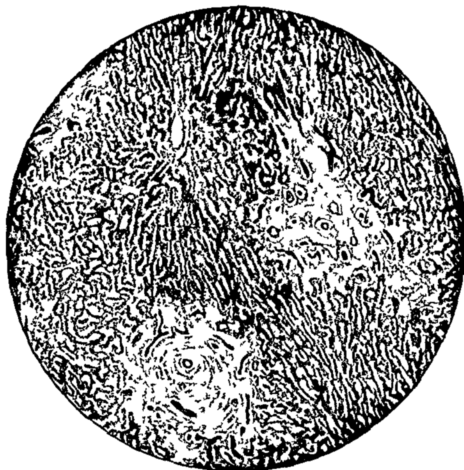


Fig 448 —Biliary cirrhosis *

irregular episodes of *fever* occur at varying intervals *pruritus* is intense and evidences of *hemorrhage* are soon encountered

Laboratory Data —The laboratory findings are those of a posthepatic or obstructive jaundice (p 1953), there are large amounts of *bilirubin* in the urine the *stools* are acholic During acute phases of the disease there may be *leukocytosis* and *anemia* Liver function tests reveal little deviation from the normal

Diagnosis —The differentiation between portal and biliary cirrhosis is suggested by Table 125

* MacCallum Textbook of Pathology

See also *Jaundice* (p 1951) *Hepatomegaly* (p 1973)

Prognosis—The course of a biliary cirrhosis is progressively unsatisfactory The patient may develop a hemorrhagic tendency with episodes of bleeding the febrile features may dominate the clinical picture there may be suggestion of an associated portal cirrhosis with advancing cholemia but in no instance can the progress of the disease be altered by therapy

Treatment—In contrast to the conditions that prevail in a portal cirrhosis dietotherapy and the administration of vitamins offer little relief from the manifestations of a biliary cirrhosis

Because of the obvious relationship of the disease to foci of infection attention is directed toward possible sites A thorough survey is required of the nose throat and paranasal sinuses antra and sphenoids are lavaged

TABLE 125—DIFFERENTIATION OF PORTAL AND BILIARY CIRRHOSIS

	Portal Cirrhosis	Biliary Cirrhosis
Age	Adults	Adolescents
History	Alcoholism and vitamin deficiency previous hepatitis	Recent respiratory infection or attack of abdominal pain
Jaundice	Late orange hue	Early olive green
Liver	Small	Enlarged
Spleen	Somewhat enlarged	Greatly enlarged
Collaterals	Caput medusa	None
Ascites	Present	Rare
Hemogram	Anemia	Leukocytosis
Clubbed Fingers	Rare	Common
Fever	Rare	Frequent
Response to Treatment	May be excellent	Poor

before the investigation is terminated any demonstrable focus is eliminated or eradicated on slight suspicion

If there is a suggestion of suppuration in the biliary passages an *exploratory laparotomy* is worthy of consideration this may be preceded by a course of systemic chemotherapy using *streptomycin* (p 103) and *penicillin* (p 106) either alone or in combination

HEMOSIDEROSIS

Hemosiderin and iron pigments are deposited in coarse granules in the parenchymal cells of various organs including the liver the disturbance is a result of *excessive hemolysis* in *chronic heart failure* (p 941) and *malaria* (p 507)

Other than enlargement of the liver there are no clinical symptoms or signs of hemosiderosis The condition has no important significance and does not require special therapy

HEMOCHROMATOSIS (BRONZE DIABETES PIGMENTARY CIRRHOSIS)

Hemochromatosis is a rare and serious metabolic defect that occurs almost exclusively in *adult males* as a result of the deposition of iron and copper pigments Characteristic discolorations of the skin and internal organs are produced the liver is the site of a hypertrophic cirrhosis and degenerative phenomena are seen in testes and pancreas

Pathogenesis—The origin of hemochromatosis has not yet been elucidated The amount of stored iron represents the total ingested in a lifetime suggesting that the defect is an inability of the liver to carry out its metabolic function with reference to this mineral A second clue as to the origin of the condition is afforded by the increased incidence in *metal workers* and those who imbibe wines that have been stored in metallic vats

Pathology—In hemochromatosis the pigmentary deposits present are *hemosiderin hemofuchsin* and *copper* In contrast to the coarse granules of hemosiderosis (p 1975) the pigmentary precipitations in hemochromatosis are finely diffused Beside the metallic deposits the liver shows considerable degeneration of the parenchyma and replacement by connective tissue in the manner of a *hypertonic cirrhosis* (p 1972) Similar pathologic changes are observed *in the testes and pancreas*

Clinical Manifestations—The first suspicion of hemochromatosis arises when *pigmentary changes* are noted in the skin and sclera the former assumes a slate blue color while the latter appears yellow brown After an interval the sufferer notes fatigability and debility Involvement of the gonads is reflected by loss of pubic and axillary hair sexual debility impotence and testicular atrophy (p 2405) pancreatic disturbances cause *glycosuria* and *hyperglycemia*

Laboratory Data—The diagnosis of hemochromatosis is established by *biopsy* of the skin and treatment of the section with stains designed to bring out the iron pigments

Diagnosis—See *Jaundice* (p 1951)

Treatment—The treatment of hemochromatosis is symptomatic *Androgen* (p 2401) is administered for the relief of the gonadal features an attempt is made to control the diabetes by diet and *insulin* but difficulties are encountered due to the ease with which insulin shock (p 1241) is produced

Under optimal conditions the patient with hemochromatosis may survive for ten to fifteen years following the onset of symptoms

BANTI S SYNDROME (HEPATORENAL FIBROSIS CONGESTIVE SPLENOMEGALY SPLENIC ANEMIA)

Banti s syndrome is characterized by chronic enlargements of *liver* and *spleen anemia* and *leukopenia* It was Banti s belief that his disease was primarily splenic with a terminal hepatic cirrhosis Most pathologists of the present era are dubious concerning the specificity of the syndrome they disagree with Banti s concept of its evolution and regard the disease as another manifestation of portal cirrhosis or obstruction due to thromboses of portal and splenic veins cavernoma of the portal vein or congestive splenomegaly with portal hypertension

Clinical Manifestations—The clinical features of Banti s syndrome are heralded by *abdominal pain* due to the splenomegaly *weakness* caused by the anemia *hematemesis jaundice* or *ascites* resulting from the portal hypertension and/or obstruction

The Banti Stages —According to Banti s description three phases are recognized In the first stage lasting three to ten years splenomegaly and anemia are encountered the second stage of one to three years duration features hepatomegaly the final act adds jaundice ascites and hemorrhage with shrinkage of the liver The hemogram is not specific the anemia is hypochromic and is associated with a leukopenia and a relative lymphocytosis

Diagnosis —See *Jaundice* (p 1951) *Splenomegaly* (p 1129)

Treatment —Treatment is symptomatic and follows the principles of management in *portal cirrhosis* (p 1972) *splenectomy* is ill advised but may *be advocated as a measure of desperation*

HEPATOLENTICULAR DEGENERATION (WILSON S DISEASE)

Wilson s disease consists of the inexplicable association of *cirrhosis of the liver* and symmetrical degeneration of the *putamen* and *caudate nucleus* (p 1418) Hepatolenticular degeneration is both *hereditary* and *familial* suggesting some innate error of metabolism in a few instances the syndrome has occurred in patients exposed to *manganese* (p 755)

Clinical Manifestations —The clinical manifestations of the disturbance are first observed in the congenital variety between the ages of ten and twenty five In its first or *hepatic phase* the patient presents the combination of fever vomiting diarrhea and epistaxis examination reveals *jaundice ascites* the *Fleischer Kayser corneal ring splenomegaly* and *hepatomegaly*

The second stage is one of intermittence with relative well being and shrinkage of the liver and spleen In the third and final stage the presenting *neurological signs* consist of *rigidity contractures tremors* and *choreiform* or *athetotic movements* the pyramidal tract is intact and there are no sensory changes

Course and Treatment —The acute type of the disease is febrile with rapid deterioration leading to death In the chronic type the patient may survive for many years in a state of invalidism

A diet of high protein high carbohydrate and low fat has given some encouraging results

PARENCHYMATOUS DEGENERATION OF THE LIVER

Cloudy swelling of the liver must occur with great frequency The mere presence of fever is sufficient to produce parenchymatous changes (p 7) in the liver cells as revealed by autopsies on patients who have succumbed to any infectious disease

Cloudy swelling of the liver has no immediate clinical significance In the vast majority of instances the lesion is reversible and there is complete restitution to normal A cirrhosis may result however when the metabolic disturbance is prolonged or repeated

FATTY INFILTRATION OF THE LIVER

Large amounts of fat may be deposited in the liver cells as *storage material* in obese patients (p 7) Following various types of hepatic injury *lipoidal infiltrations* appear as evidences of a degenerative process since necrotizing parenchymal cells apparently take up fat when they are

damaged So called *fatty degeneration* accompanies phosphorus and chloroform poisonings (p 4068) arsenical hepatitis the infectious types of jaundice and uncontrolled diabetes in the young

The fatty liver is palpable but not tender functional tests may or may not reveal abnormalities abdominal pain is encountered from stretching of the capsule jaundice does not occur

The treatment schedule follows the principles enunciated in cirrhosis (p 1971)

HEPATIC AMYLOIDOSIS (LARDACEOUS LIVER)

Amyloid is often deposited in the liver as the result of chronic disease particularly with prolonged suppuration similar material is found in blood vessels the spleen and kidneys Amyloidosis is most frequently observed in long standing *osteomyelitis* (p 2936) *arthritis* (p 2910) *malignancy* (p 572) or *tuberculosis* (p 252)

Amyloidosis is suspected in chronic disease when there is painless enlargement of liver and spleen *waxy casts* may be found in the urine there is retention of the *congo red* test dye Jaundice and ascites do not occur since the deposits do not invade the hepatic parenchyma or cause *cirrhosis*

There is no way by which amyloid deposits can be dissipated a casein free diet has been recommended on purely hypothetical grounds

GLYCOGEN INFILTRATION (GLYCOGENOSIS VON GIERKE S DISEASE)

Deposits of glycogen occur in the liver as the result of a congenital and familial metabolic anomaly that appears in infancy The precipitates are also seen in the heart kidneys and spleen

Clinical Manifestations —Von Gierke s disease is suspected in children who develop a *huge abdominal swelling* due to the presence of a *gigantic liver* There are usually accompanying neurologic manifestations such as *internal hydrocephalus* (p 1410) *infantilism* (p 692) *convulsions* (p 1519) and *idiocy* (p 1332) Jaundice ascites and splenomegaly are not conspicu ous if present at all

Laboratory confirmation of some defect in sugar metabolism is afforded by *fasting hypoglycemia* and the failure of the blood sugar level to rise in normal fashion following the injection of epinephrine the *stools* contain large amounts of *undigested starch (amylorrhea)* It is thought that the disease represents an intracellular disturbance of the phosphorylase phos phatase system resulting in abnormal stability of glycogen

Course and Treatment —*The afflicted child usually dies of an intercur rent infection* Large doses of vitamins may be given but treatment is ineffectual

THE HEPATIC MANIFESTATIONS IN THE LIPOIDOSES AND XANTHOMATOSES

The group of lipoidoses includes a variety of congenital metabolic anomalies which are variously described as *Gaucher s disease* (p 1133) *Nie mann Pick s disease* (p 1134) *Hand Schuller Christian s disease* (p 1137) the *xanthomatoses* (p 1136) and *Tay Sachs disease* or *amaurotic family idiocy* (p 1333) The first two of these syndromes are characterized by *hepatosplenomegaly* due to the presence of lipoid material formed in in

termediary metabolism and deposited in the reticular cells In xanthomatosis the reticular cells take up lipids from the blood

Splenectomy is worthy of consideration in these diseases if there is marked bleeding or abdominal discomfort due to the enlargement of the viscus

INFECTIONS

The liver is involved in systemic infections such as *yellow fever* (p 477) *Weil's disease* (p 360) *infectious mononucleosis* (p 466) the generalized *septicemias* (p 54) and *lobar pneumonia* (p 2171) In each of these conditions the hepatitis is a secondary consideration and treatment is directed to the more fundamental disorder

The more local forms of infectious hepatitis include catarrhal jaundice liver abscess hepatic syphilis hepatic distomiasis and echinococcus disease

CATARRHAL JAUNDICE (INFECTIOUS JAUNDICE CATARRHAL ICTERUS)

Catarrhal jaundice is a specific infectious disease It is the commonest form of febrile icterus and may occur in isolated or epidemic form

Bacteriology —The causative agent of catarrhal jaundice has been identified as a specific virus excreted in the feces of persons afflicted with the disease It may be transmitted in contaminated water but is attenuated by an exposure of 30 minutes to chlorine concentrations of 15 parts per million

Physiological Phases —Physiological investigations confirm the clinical impression that the infection is specific and reveal three distinct stages In the *obstructive phase* there is an increasing level of serum bilirubin and an absence of urobilinuria the *critical period* is marked by decrease of serum bilirubin and increased urobilinuria the *stage of recovery* reveals a restitution towards the normal

Pathology —It is the general belief that the primary disturbance in catarrhal jaundice is a *gastroduodenitis* with ascending infection into the biliary ducts Foci of degeneration and necrosis appear in the parenchyma of the liver and a cholangitis involves the finest biliary radicles The pathological picture corresponds in its distribution to the lesion of *biliary cirrhosis* (p 1972) The latter which also occurs in the relatively young may represent a fibrotic stage of the catarrhal infection

The occasional demonstration of a hemogram of *infectious mononucleosis* (p 466) and the similar serologic reactions suggest that the two diseases may be closely related *each produces false positive tests for syphilis* (p 337) in catarrhal jaundice a *heterophile reaction* (p 468) may be obtained in the higher dilutions

Epidemiology —Catarrhal jaundice is transmitted through fecal contamination In human experiments the oral administration of pooled specimens of feces obtained from patients during pre icteric icteric and post icteric phases of their illness reproduced the disease in approximately 26 days In addition to human transmission catarrhal jaundice also may be produced by contaminated food water and inanimate objects The period of highest infectivity appears to be during the prodrome

Clinical Manifestations —Catarrhal jaundice characteristically affects children and young adults who are otherwise in excellent health and who have not been exposed to known hepatotoxic influences (p 1963)

Prodromes—The infection is introduced by vague intestinal discomforts including anorexia nausea vomiting mild diarrhea epigastric discomfort and intolerance for fats Occasional arthralgias are noted Percussion tenderness is present over the liver and the right costovertebral area The liver may be palpably enlarged and there may be cervical lymphadenopathy Particularly arresting is the history of exposure to a similar ailment

Jaundice—After several or more days of nondescript illness the cornea appears icteric the urine is stained with bile pigment the stools appear light in color but are not actually acholic a hyperbilirubinemia is demonstrable and the laboratory evidences of hepatitis (p 1947) are obtained

Diagnosis—The diagnosis of catarrhal jaundice is made on clinical grounds *toxic hepatitis* (p 1963) is distinguished by the history of exposure to a hepatotoxin *spirochetal jaundice* (p 360) is of rare occurrence in North America and presents positive laboratory phenomena in *yellow fever* (p 477) there is the history of mosquito bite and of similar infections in the immediate vicinity *Serum jaundice* (p 82) follows transfusion or injection of contaminated material and has a longer period of incubation (60 to 120 days)

Course—Catarrhal jaundice may last for three weeks or three months In the milder examples the temperature falls to normal jaundice recedes and recovery is apparently complete although the patient may note a certain amount of lethargy for a greater or lesser period of time

In the more severe examples fever persists and increases jaundice deepens and the laboratory data suggest a possible transition to the stage of *acute yellow atrophy* (p 1968) However even the most severe examples of catarrhal jaundice eventually show evidences of improvement and progress to complete clinical recovery

Treatment—Infectious jaundice may be prevented by intramuscular injection of gamma globulin if given earlier than six days before the onset of symptoms The agent has no curative value and the passive immunity persists for only two months Active therapy involves prolonged bed rest a full diet and injections of crude liver extract (p 1967) and menadione (p 630)

LIVER ABSCESS

Hepatic suppuration may be produced by many pathogens and may result from a variety of different pathological processes Multiple abscesses are usually pyogenic large solitary lesions are produced by amebae helminths and infections of the gallbladder

Etiology and Pathogenesis—The most frequently observed causative lesions are *suppurative diseases of the gallbladder and bile ducts* (p 2007) when infection travels by direct extension in *pylephlebitis* (p 1961) usually of appendiceal origin (p 1881) the invaders are carried by the portal vein in *septicemias* the bacteria travel through the hepatic arteries abscesses that result from *amebic and echinococcus disease* (p 1983) or *hepatic distomiasis* (p 1982) are propagated through the bile duct

Clinical Manifestations—The clinical manifestations of abscess of the liver usually occur while the primary inflammatory process is still active but they may not appear for many years

Para infectious Abscesses—The para infectious examples of hepatic suppuration are illustrated in *pylephlebitis* (p 1961) of appendi[illegible] igin or

a suppurative *cholangitis* (p 2010) The patient becomes more toxic the fever assumes the character of a sepsis with wide variations and chilling the deterioration of the clinical condition seems not to be explicable on the basis of any increase in the manifestations of the fundamental disorder

Hepatic suppuration is suspected when the patient reports *pain in the right upper quadrant* (p 1050) since the right lobe is more frequently involved The physician elicits jar tenderness which had not been previously present roentgenographic examinations reveal impaired motility and considerable elevation of the right leaf of the diaphragm and there may be sufficient displacement to produce an atelectasis of the right lower lobe of the lung (p 2052) The simulation of pulmonary disease is often furthered by the appearance of a *sterile sympathetic pleural effusion* (p 2222)

The presence or absence of *jaundice* depends on factors of chance If a main biliary duct is compressed sufficient bilirubin enters the biliary channels to produce a clinical icterus otherwise jaundice may be deceptively absent

Postinfectious Abscess—The postinfectious hepatic abscess is usually unilocular Most often it is a manifestation of *amebiasis* (p 523) less frequently it is the result of *actinomycosis* (p 489) *distomiasis* (p 1982) or *hydatid disease* (p 1983)

The symptoms of the unilocular abscess are variable It may become manifest through localized pain or an enlargement of the liver At times the condition is suspected without objective physical findings in the investigation of an otherwise inexplicable jaundice or a cryptogenic sepsis

Laboratory Data—Hepatic abscesses are usually accompanied by pronounced leukocytosis Blood cultures are usually sterile even when the course is hectic a significant eosinophilia may accompany protozoal and helminthic disease Stool examinations may reveal the presence of amebae the ova of distomiasis or the hooklets of hydatid disease (p 1983)

Course—The course of hepatic suppuration is unpredictable The abscess may become walled off and remain silent for innumerable years it may burst into the pleura or the lungs creating an *empyema thoracis* (p 2219) a *hepatopulmonary fistula* or *lung suppuration* (p 2219) Should the abscess point into the peritoneal cavity it gives rise to a generalized or a localized purulent extension (p 2215)

Hepatic suppuration may cause hematogenous metastases in the *lungs* (p 2214) or *brain* (p 1468) these may give rise to immediate symptoms or they may lie dormant for long periods of time

Diagnosis—The practitioner can at best only suspect the diagnosis of hepatic suppuration The demonstration of its etiology depends upon therapeutic tests with *emetine* and *sulfonamides* *needle aspiration* and *operative findings*

Treatment—The management of liver abscess combines chemotherapy and a surgical attack

Chemotherapy—On suspicion of the presence of a liver abscess the patient is given a therapeutic test with *emetine* (p 88) whether or not amebae are demonstrable in the stools Concurrently or later streptomycin (p 104) and/or penicillin (p 106) are administered parenterally Sulfonamides may be added (or substituted) if previously used agents appear ineffectual

Surgery—With failure of chemotherapy the consulting surgeon is re

quested to take the patient to the operating room the most suspicious area preferably posteriorly is needled for the demonstration of pus from an abscess cavity Should purulent material be obtained, the needle is kept in place and an attempt is made to incise and drain the area without soiling pleura or peritoneum If either of these cavities is entered a second stage procedure is attempted after several days in the hope that adhesions will have formed to protect the main cavity

The fluid that is withdrawn is examined culturally and by direct smear indicated chemotherapy is continued in amebic or pyogenic infections If a focus is demonstrable in the gallbladder or the larger bile ducts the question of further surgical therapy is discussed with the consultant

HEPATIC SYPHILIS

See p 1964

HEPATIC AMEBIASIS

See p 525

HEPATIC DISTOMIASIS

At least two varieties of the schistosomes exhibit an elective affinity for the liver *Clonorchis sinensis* and *Fasciola hepatica* pass through a complicated life cycle terminating in hepatic pathology

Distribution —The *C sinensis* is indigenous to Japan the Kwangtung province of South China Formosa and French Indo China The *F hepatica* is observed in Chile Argentina Venezuela Cuba Puerto Rico Greece France Hungary Italy Roumania Russia Scotland Turkey Turkestan Syria Algeria French Somaliland and Australia

Life Cycle —The adult *C sinensis* lives in the bile ducts of man dog cat and other fish eating mammals Eggs containing the mature *miracidia* pass with the bile into the intestines and are expelled with feces In water the eggs hatch and are taken up by certain *snails* which act as first intermediate hosts After a complicated evolution within the snail myriads of *cercariae* emerge and seek a second intermediate host which is usually a species of *fresh-water fish* Here the cercariae penetrate under the skin and become encysted Man or other fish eating mammal becomes infected when raw or inadequately cooked food is eaten

Within the stomach and duodenum the cyst wall is digested the liberated *metacercariae* enter the common bile duct and work their way into the smaller biliary radicles where they grow to adult life

Clinical Manifestations —Many apparently healthy persons harbor liver flukes Quite possibly symptoms are produced only when the parasites are produced in tremendous numbers The clinical manifestations may be *local* or *systemic* the liver is sometimes enlarged and sensitive to pressure pain may be noted in the right hypochondrium or the epigastrium occasionally jaundice is produced a bleeding tendency may be manifested by epistaxis or bloody diarrhea In the more severe infections ascites swelling of the lower extremities anemia and a general cachexia are noted

Diagnosis —The diagnosis of hepatic distomiasis is made from the finding of the *small brown operculated eggs in the duodenal content or the stool* (p 3731)

Treatment—The liver fluke is resistant to treatment *antimony compounds* (p 132) may be employed as in intestinal distomiasis (p 1898) *hexamethyl rosanilines* have been tried by oral administration using 30 mg on alternate days intravenous injections of 40 cc of 0.5 per cent solution have also been used with reported success

ECHINOCOCCUS OR HYDATID DISEASE OF THE LIVER

The echinococcus is a tapeworm (p 537) capable of producing huge hydatid cysts of the liver

Distribution—*Echinococcus granulosus* is common in regions of Europe Iceland Argentina, Paraguay and Australia In the United States human infections are rare but the taenia is demonstrated in timber wolves and moose

Life Cycle—The adult tapeworm lives in the small intestines of the dog wolf jackal and other related species The larval stage of *hydatid* occurs in the liver and lungs of numerous species of mammals including sheep oxen pigs and lambs The *adult tapeworm* is minute and measures less than 5 mm in length The *head* is 0.3 mm in breadth and has a double row of *hooklets*

The hydatid form develops by liquefaction of the interior of the larva after it has invaded the tissue it grows to considerable size and has an external laminated *cuticle* and an internal parenchymatous or *germinating layer* The final forms are *brood capsules* which contain the characteristic *scolices* each of which may develop into an adult worm if ingested by the dog which is its proper host the eggs of the worm are disseminated by dogs which harbor adult forms the parasite is transmitted to man through oral transference

Clinical Manifestations—Hydatid cysts occur most frequently in the *liver* but are also found in the *lungs pleura abdominal organs* the *nervous* and *circulatory systems* Most often the disturbance is *asymptomatic* unless a *tumor mass* is produced in the hepatic region On rare occasions the first indication of the infestation follows rupture of the cyst or secondary infection of the wall with suppuration

Diagnosis—In areas where echinococcus disease is frequently observed an enlarged mass in the liver region arouses the suspicion of the medical advisor A *skin test* (p 59) using fluid obtained aseptically from hydatid cysts of cattle has proved very satisfactory a *complement fixation test* (p 59) and a *precipitation reaction* (p 59) are also available The definitive diagnosis is established by finding *scolices* or *hooklets* in material obtained by operation or aspiration

Treatment—Echinococcus disease is treated *surgically* An attempt is made to remove the cysts where possible Under other circumstances the lesion is *marsupialized* Unfortunately surgical treatment is not always successful and may serve to disseminate the disease If the cyst has ruptured into a serous cavity grave symptoms may ensue *Roentgen therapy* has been employed to favor absorption of hydatids but the value of this form of treatment has not been definitely established *Chemotherapy* unfortunately is of no value

CHAPTER 98

THE BILIARY DUCTS AND GALLBLADDER METHODS OF DIAGNOSIS AND TREATMENT CLINICAL DISTURBANCES

ABNORMALITIES *of the biliary ducts and the gallbladder present frequent* clinical problems Cholelithiasis (p 1997) is present in 5 to 6 per cent of adults who come to postmortem examination for any cause while an estimated 90 per cent of these are apparently asymptomatic the remaining 10 per cent make up a significant proportion of patients who consult their practitioner for intra abdominal and digestive complaints

ANATOMY

See p 3558

PHYSIOLOGY

Bile is secreted by the liver cells and flows into the main hepatic ducts which join to form the common channel The hepatic secretion under normal circumstances is diverted into the cystic duct to the gallbladder where it is stored and concentrated The altered gallbladder bile at the proper time passes out through the cystic duct and thence by way of the common duct, to the lumen of the duodenum Under unusual circumstances the gall bladder may be by passed and the hepatic secretion travels directly into the bowel

Bile—There is considerable confusion in phys ology and clinical medicine regarding the use of the word bile In its strictest sense bile refers to the *complete hepatic secretion* which includes bile salts bilirubin biliverdin and urobilinogen Unfortunately the word is often used to mean one of its constituents when the clinician asks whether there is bile present in the stool he is actually referring to *urobil nogen* when inquiry is made concern *ing the presence of bile in the serum or the urine the reference is to bilirubin the bile pigment*

The B l ary Co st tue ts in the Normal Body Fluids—Bile is found normally in the biliary radicals the gallbladder and the duodenum

B lirubin is present in the bile in the intestines and in traces in normal human serum (0 1 to 0.5 mg per 100 cc) it is absent from normal stool and urine

Urobilinogen is present in the bile in the intestines in the stool and in the portal blood but does not appear in the urine or the serum of the systemic circulation

Urob lin is present in the stool it occurs in minute amounts in normal urine but should not appear in the biliary passages the intestines the portal blood or the serum of the sys temic blood

Compos t on of Li er and Gallbladd r B l—On leaving the hepatic cells b le is a gol len yellow fluid of low viscosity It is composed of 97.5 per cent *water* and 2.5 per cent

TABLE 1 6—THE BILIARY CONSTITUENTS IN NORMAL BODY FLUIDS

	Bilirubin	Urobilinogen	Urobil n
Bile	+	+	0
I testine	±	+	0
Stool	0	+	+
Urine	0	0	Traces
Portal Blood	+	+	0
Systemic Blood	Traces	0	0

dissolved sol ds the latter include *mucin bile pigments bile salts fatty acids cholesterol lecith n f t* and *ino ganic salts*

W thin the gallbladder l ver bile is concentrated tenfold by absorption of water and salts the product becomes dark and thick and the degree of concentration is evidenced by the higher content of bilirubin Gallbladder bile is made more viscous by the addition of mucin it is somewhat less alkaline than liver bile

See *Biliary Drainage* (p 3726)

Bile Salts—The b le salts are the sod um salts of *glycocholic* and *taurocholic acids* the latter are formed from the combination of the amino acids *taurine* and *glycine* with cholic acid which contains the phenanthrene ring and is derived from cholesterol

The bile *acids and their salts are formed in the liver and pass into the intestine as con* stituents of bile They ass st in the intestinal absorption of fatty acids and cholesterol they are largely reabsorbed (85 per cent) into the portal blood and returned to the liver where they are used anew a small amount (15 per cent) is excreted in the feces

B liary Lipids—Fatty acids neutral fat phosphatids and cholesterol constitute the lipid fraction of the bile sol ds Normal bile contains 20 to 200 mg of free cholesterol per 100 cc but cholesterol esters are absent Cholesterol is held in solution by the presence of an optimal concentration of bile salts disturbances in the normal rat o of b le salts to cholesterol lead to precipitation of cholesterol and the formation of *calculi* (p 1997)

Bile P gments—The color of the bile is produced by the p gments *bil rubin* and *biliver d n* these comprise 15 per cent of the biliary solids

B lirubin is a product of the breakdown of hemoglobin in the process of red blood cell destruction by the cells of the reticulo-endothelial system One gram of hemoglobin yields about 40 mg of bilirub n the plasma normally contains 0 1 to 0.5 mg per 100 cc

The *extrahepatic* formation of bile pigment is so extensive that bilirubin continues to be formed at a rate *approximating the normal when experimental animals are deprived of liver and spleen* The extrahepatic bilirubin upon reaching the liver cells is excreted unchanged into the bile this mechanism is operative in prehepatic jaundice (p 1959)

Urobilinogen and Urobilin—In the intestines bilirubin is reduced by bacterial action to urobilinogen the urobilinogen is then excreted in the stool or oxidized to urobilin and excreted as such

A portion of the urobilinogen is resorbed into the portal circulation returned to the liver and re excreted in the bile Any excess of urobilinogen that escapes into the general circulation is excreted by the kidney as urobilin

Functions of the Bile—The presence of bile in the intestines is necessary for the maintenance of life the known functions of bile are the following

1 Assistance with the digestion and absorption of *fat*
2 Activation of *steapsinogen*
3 Co ferment activity in connection with the activated fat splitting enzyme
4 An emulsifying agent for *fat*
5 Antiputrefactive activity by enhancing the effects of the proteolytic and amylolytic enzymes of the intestines
6 Stimulant of *peristalsis*
7 Carrier action to assist the passage of fatty acids through the mucosa
8 Aid in the absorption of the *fat soluble vitamins* D E and K
9 Aid in the elimination of *bile pigments bile acids cholesterol* and *lecithin*
10 Aid in the *excretion* of the salts of the *heavy metals* and *drugs* such as quinine atropine strychnine nicotine the salicylates benzoates and the dyes used in estimations of liver function
11 Cholagogue stimulating the flow of bile from the liver
12 Prevents precipitation of cholesterol and fatty acids in the gallbladder

Functions of the Gallbladder—*The gallbladder serves as a reservoir for bile* which it concentrates To gallbladder bile is added a secretory mucus after which the product is propelled into the intestines during the proper phase of digestive activity

The Reservoir Function of the Gallbladder—Bile is secreted by a continuous process but the flow into the duodenum varies with the amount and character of the food it is increased during digestion and decreases between feedings During the latter phases bile is diverted into the gallbladder by contraction of the sphincter of Oddi at the duodenal end of the common bile duct *In the gallbladder it is stored until the onset of the next fatty meal*

Concentration of Bile by the Gallbladder—The liver puts forth 500 to 1200 cc of bile daily the estimated output of gallbladder bile approximates but 10 per cent of the total of liver bile so that extensive resorption of water and inorganic salts must occur through the wall of the sac

The pathological gallbladder is not able to concentrate liver bile as best demonstrated in cholecystograms It may even absorb some of the constituents *such as the bile salts and cholesterol* which are normally concentrated *When the gallbladder is surgically removed* the bile ducts vicariously assume its functions liver bile is somewhat concentrated and a mechanism is provided by which the product is delivered into the duodenum when fatty foods are present

Gallbladder Secretion—The normal gallbladder excretes 20 cc of a mucoid nucleoalbumin each day With acute irritation of the wall the amount of secretion is increased (*white bile*) Under other pathologic conditions such as hydrops the wall of the gallbladder may elaborate a fluid that contains significant amounts of cholesterol favoring the deposition of gallstones (p 1997)

Biliary Kinetics—The flow of bile is dependent upon an interrelationship between the sphincter of Oddi and the musculature of the gallbladder These structures receive reciprocal innervation a stimulus which causes contraction of the one provides for relaxation of the other

The stimulus for bile flow *is the presence of fats and fatty substances in the upper* bowel the pathway is hormonal due to the elaboration of *cholecystokinin* an enzyme which has been sufficiently refined so that intravenous injections are demonstrated to produce powerful contractions of the biliary musculature In the absence of chemical stimuli in the

duodenum the sphincter is closed bile is diverted into the gallbladder which then fills preparatory to expulsion at the time of digestion

FILLING OF THE GALLBLADDER—The regulation of bile flow depends on the circular and longitudinal muscle fibers which form the sphincter of Oddi situated in the papilla of Vater The circular fibers of the sphincter are contracted when the stomach is empty pressure increases in the common duct and forces open the heisterian valves of the cystic duct permitting bile to enter the gallbladder This mechanism forms the basis of cholecystography when the iodine-containing dye present in the bile enters the gallbladder for later concentration and excretion

EMPTYING OF THE GALLBLADDER—When the upper intestine contains food products which require the presence of bile salts for their digestion and absorption cholecystokinin is secreted and exerts its stimulus upon the musculature of the gallbladder the sac contracts the sphincter of Oddi is relaxed and bile passes through the duct system and into the intestines

Normally the expulsion of bile begins within ten to fifteen minutes after the ingestion of the fat-containing meal the normal gallbladder is approximately two-thirds empty at the end of the first half hour it continues to drain for another two-and a half hours but never completely empties

The gallbladder exhibits *tonic contractions* which last twenty five to thirty minutes and momentary *rhythmic motions* which may occur in the absence of the tonic element With a tonic contraction the pressure within the gallbladder is raised to about 30 cm of bile and there is a partial evacuation of the content rhythmic contraction produces only slight increases in intra gallbladder pressure The overdistended gallbladder may be drained by elastic recoil of its muscular tissue rather than by active contraction resulting from the presence of the hormone

Disturbances in bile circulation are of great clinical importance and are elsewhere discussed under the heading of *Biliary Dyskinesia* (p 2007)

Cholagogues—In addition to the physiological hormone pharmacological cholagogues augment the flow of bile into the duodenum The drugs that are potent include the pituitary extracts pilocarpine physostigmine choline histamine niacin calomel and magnesium sulfate Atropine amphetamine and the nitrites relax the gallbladder and favor retention

SPECIAL DIAGNOSTIC INVESTIGATIONS

A variety of special methods are available for investigation of the gall bladder and the biliary passages No one method furnishes absolute evidence of the nature of the pathologic condition but the overall picture quite clearly delineates the lesion and tends to aid in the decision as to the wisdom of surgical or nonsurgical therapy

Physical Examination—Occasionally an enlarged gallbladder containing huge stones is palpable chronic hydrops of the gallbladder signifies extra biliary obstruction (Courvoisier s law) as in carcinoma of the head of the pancreas (p 1943) localized involuntary muscle rigidity intimates that there is a pericholecystitis with a peritoneal reaction

Urine—*Bilirubinuria* (p 1951) is definitive evidence of the presence of a posthepatic or obstructive jaundice the additional presence of large amounts of *urobilinogen* (p 1948) in the urine suggests superimposed biliary tract infection or increased hemolysis

Stool—Bulky stools containing large amounts of *fat* but no *urobilinogen* (acholia) indicate that the biliary passages are totally obstructed Increased amounts of urobilinogen suggest excessive hemolysis (p 1060)

Duodenal Contents—The examination of the duodenal contents is discussed at length elsewhere (p 3726) If *red cells* and *pus* are demonstrable in a cleanly obtained specimen there must be bleeding and suppuration within the biliary system *cholesterol crystals* suggest the presence of concretions (gallstones) failure to obtain bile occurs in a complete stoppage

Slightly more controversial are the results of *duodenal drainage* follow

ing the instillation of test substances such as olive oil or 33⅓ per cent epsom salts The importance of A B and C bile is discussed elsewhere (p 3727) *Bacteriological studies* of specimens obtained by sterile technic occasionally reveal the nature of the invading organism (streptococci typhoid or colon bacilli)

Blood Examination—*Hyperbilirubinemia* (p 1951) and elevation of the icterus index are demonstrable in any type of obstructive jaundice the *van den Bergh reaction* (p 1947) is directly positive *until damage occurs* to the liver cells when the indirect test becomes positive *cholesterol and cholesterol ester* (p 1948) figures are increased in obstructive jaundice *serum phosphatase* (p 729) reaches high values with posthepatic jaundice the *cephalin cholesterol flocculation test* (p 1949) is not changed until

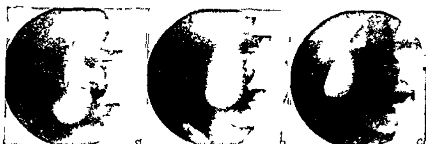


Fig 444—Normal cholecystographic response patient of average size *a* Fourteen hours after taking dye *b* sixteen hours after taking dye *c* twenty hours after taking dye and forty five minutes after taking fatty meal*



Fig 445—Normal cholecystographic response of heavy patient (250 pounds) Note high lying gallbladder *a* Fourteen hours after taking dye *b* sixteen hours after takin dye *c* twenty hours after taking dye and forty five minutes after taking fatty meal

liver cell damage has occurred the *prothrombin time* (p 1109) is prolonged and injection of vitamin K fails to correct this abnormality

Leukocytosis points to infection as a cause or complication of the obstruction elevation of the *nonprotein nitrogen* level indicates approaching cholemia fall of blood calcium occurs in *hemorrhagic complications*

Diagnostic Roentgenography—Diagnostic radiography is of great importance in the interpretation of diseases of the gallbladder The *scout film* often reveals calcium stones or the characteristic signet ring radiopaque shadow of a mixed stone which contains a *nucleus* of cholesterol or bile pigment and a *peripheral shell* of calcium Occasionally calcification of the gallbladder itself is revealed

* Walters and Snell *Diseases of the Gallbladder and Bile Ducts*

Cholecystography—Contrast cholecystography (p 2000) or visualization of the gallbladder is accomplished by administering a dye which is excreted in the biliary secretion Observations are made of the filling shadow its concentration and the expulsive efforts following the administration of a fat meal

The test cannot be performed with safety in the presence of jaundice hence it has distinct limitation In the nonjaundiced patient however the films are of tremendous value

Cholangiography—Cholangiography may be necessary during or after operation lipiodol or hippuran is injected into the common bile duct through a T tube using only slight pressure Radiography may then reveal local obstructive lesions due to calculi strictures neoplasms abnormalities of the pancreatic duct or spasm of the sphincter of Oddi

Exploratory Laparotomy—The final diagnostic measure is exploratory laparotomy for direct inspection and palpation of the gall sac and the common duct Bile may be withdrawn by direct puncture from the gallbladder if liver abscess is suspected the organ is needled in suspicious areas it may be necessary to open the common duct for probing

SPECIAL METHODS OF TREATMENT

The treatment of biliary tract disease is accomplished by dietotherapy duodenal and transduodenal lavages the use of drugs and operative surgery

Diet—In diseases of the gallbladder and biliary tracts custom dictates the use of a *high carbohydrate moderate protein* and *low fat intake* (p 672) Physiological considerations however point to the importance of utilizing fats and fatty substances in order to stimulate the secretion of *cholecystokinin* and favor *expulsion of bile*

A compromise may be reached that is satisfactory to both clinician and physiologist since they agree as to the carbohydrate and protein requirements Each feeding is initiated by the ingestion of a small quantity of *fat* such as butter or olive oil but the meal is itself low in fat This plan favors drainage of the gallbladder but it does not appreciably increase the caloric intake nor too greatly elevate the level of the blood cholesterol

Supplementary doses of the *fat-soluble vitamins* A D and K are given

Duodenal Lavage and Transduodenal Feedings—The authors are among those who are unimpressed by the clinical results of duodenal and transduodenal lavages The practitioner who has observed cholecystography realizes that effective contraction of the gallbladder is accomplished by the simple fat meal under these circumstances it seems unnecessarily distressing to require the patient to swallow several feet of rubber tubing to accomplish the same result

For those who are interested in the more complicated forms of therapy reference is made elsewhere to the technics of *duodenal lavage* (p 1749) and *transduodenal feedings* (p 1752)

Drugs—In biliary tract disease drugs are used to increase the flow of bile (*choleretics*) to facilitate the emptying of the gallbladder (*cholagogues*) as *antispasmodics* for *replacement therapy* and as *antiseptics*

Choleretics—*Hydrocholeretics* are used to produce a less viscid bile which is poor in solids The indications are theoretical but the effect is

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accomplished by intravenous injections of *sodium decholin* in doses of 0 6 to 2 0 cc of 20 per cent solutions or tablets of dehydrocholic acid (0 2 gm)

Choleretics are intended for the production of increased bile flow with additional bile salt The most effective choleretics are *whole ox bile* and the *bile salts* (p 1048) less striking effects may be obtained from *acetyl salicylic acid* (p 3832) and *rhubarb* Contrary to general opinion *calomel* is not choleretic

Cholagogues—The most effectual cholagogue is fat preferably given at the beginning of the meal

Cholecystokinin—See p 1986

Bile Salts—Replacement therapy with bile salts is required in patients with external biliary fistulas (p 1992) and as an adjuvant in the treatment of vitamin K deficiencies (p 1111) The available preparations are the *natural bile salts ketochol* and *decholin* administered *in daily doses of 5* to 15 grains *oxidized bile salts* are employed in doses of 3¾ grains

When bile is lost by fistula or excluded by obstruction the *fat-soluble vitamins* and *calcium* are also utilized

Biliary Antiseptics—The prospects of effectual biliary antiseptics have brightened since the introduction of streptomycin (p 104) and penicillin (p 106) Because invaders are more often gram negative organisms sensitive to streptomycin this antibiotic holds greatest promise but both agents because of their minimum toxicity may be given in combination when the indications are urgent

Antispasmodics—The use of antispasmodics is particularly recommended in biliary dyskinesia in which there is closure of the sphincter of Oddi The favored preparations include *nitroglycerin* (p 3893) *atropine* and its derivatives (p 3875) *demerol* (p 3863) *papaverine* (p 3854) and *calcium salts* (p 3824) *Morphine* (p 3853) increases muscle spasm and is contraindicated

Surgery—The indications for surgical treatment of biliary tract disorders are increasing as operative technics are perfected and risks diminished

Indications—*Absolute* indications for operative interference include extrahepatic biliary obstruction the suspicion of neoplasm recurrent infection of gallbladder or ducts suppurative gangrenous penetrating or perforating lesions of the gallbladder acute cholecystitis and external biliary fistulas

Relative indications for surgery are present with persistent dyspepsia (p 1770) repeated episodes of biliary colic evidences of biliary cirrhosis (p 1972) a poor response to medical therapy evidences of pancreatitis and associated angina pectoris or cardiac arrhythmia

Cautions—In chronic cholecystitis without cholelithiasis and in biliary dyskinesia operative interference holds little promise and may be followed by the *postcholecystectomy syndrome* (p 1992)

Preoperative Preparation—Before operation on the gallbladder or biliary tract the *obese patient* is entitled to weight reduction A period of rest is mandatory in the *flabby middle aged individual* in order that conditions may be optimal before the anesthetic is administered

During the preliminary rest period large amounts of *carbohydrate* food are used to protect against liver damage 1 or 2 mg of *vitamin K* are in

jected each day for at least a week a course of prophylactic chemotherapy with *streptomycin* (p 104) is highly advisable if there are evidences of infection the *blood is typed* for transfusion in the event that there is excessive bleeding Provisions are made for setting up a *continuous intravenous drip* of 5 per cent dextrose in saline solution as soon as the patient has returned from the operating room and injections of streptomycin are continued

Obstructive jaundice is complicated by a bleeding tendency which is due to poor absorption of *vitamin K* from the bowel with consequent *prothrombin deficiency* as estimated by determination of the prothrombin time (p 1109) Before any operation is undertaken the deficiency should be remedied by the oral administration of vitamin K and bile salts for two to three days or by parenteral administration of vitamin K substitute The adequacy of the therapy can be checked by reestimation of the prothrombin time (p 1109) In addition *fluid electrolyte balance* should be established before any surgical procedure (p 718) and the *glycogen stores* in the liver should be raised as much as possible by oral administration of *carbohydrate or parenteral administration of glucose solution (p 3775)*

Anesthesia—The anesthetics of choice are *spinal* if local methods are to be employed and inhalations of *cyclopropane* or *ether* with curare for general anesthesia *Pre anesthetic medication* (p 3836) is accomplished by a triple dose of the favorite hypnotic given $1\frac{1}{2}$ hours before the projected procedure and a hypodermic injection of dilaudid grains $\frac{1}{30}$ and hyoscine hydrobromide grains $\frac{1}{150}$ an hour later

Types of Surgical Procedure—The common operations on the gall bladder and biliary tracts include cholecystotomy cholecystostomy cholecystectomy and choledochotomy

CHOLECYSTOTOMY—Cholecystotomy is performed for gallbladder drainage when the sac is incised or aspirated It must be followed by a secondary procedure preferably a cholecystectomy

CHOLECYSTOSTOMY—In cholecystostomy the gallbladder is drained but not removed This procedure is indicated when the patient is in poor condition and a prolonged operation may not be tolerated it is also advisable in the presence of extensive infection of the extrahepatic biliary tract with or without bacteriemia

CHOLECYSTECTOMY—Cholecystectomy accomplishes the removal of the gallbladder It is the operation of choice except under the conditions above mentioned

CHOLEDOCHOTOMY—Choledochotomy refers to incision of the common duct a procedure that is necessary for diagnosis or the extraction of an impacted common duct stone

CHOLECYST-GASTROSTOMY AND CHOLECYST ENTEROSTOMY—With common duct obstruction that cannot be relieved the palliative procedure of either *cholecyst gastrostomy* or *cholecyst enterostomy* establishes an internal biliary fistula relieves the jaundice and permits the patient a considerable amount of comfort particularly from the intense itching

Postoperative Treatment—Operations on the gallbladder and biliary passages are frequently followed by complications These include *shock fever pulmonary atelectasis* (p 2052) *local bleeding* (p 4007) *dilatation of the stomach* (p 4005) *phlebitis* (p 1123) *pulmonary embolization* (p

2086) *postoperative pneumonitis* (p 4016) continued *biliary obstruction* the *postcholecystectomy syndrome* (p 1992) *external biliary fistulas* and *strictures of the ducts*

SHOCK —Postoperatively jaundiced patients are prone to develop shock which can be controlled by transfusion If external biliary drainage has been established adequate fluid and salt intake must be maintained by the intravenous route until a full diet is tolerated since large amounts of salt are lost daily in the biliary drainage Not infrequently the *sodium loss* (p 729) in the biliary drainage on the fifth to eighth day after operation causes anorexia dehydration and a shock like picture with low blood pressure and a thready rapid pulse This condition dramatically responds to administration of saline intravenously

FEVER —Postoperative temperature elevation as high as 103 and 104 for twenty four to forty eight hours is not uncommon after common duct surgery It need cause no undue concern if there is no evidence of a pulmonary or wound complication and if the urinary output is adequate *Oliguria or anurias call for* prompt intravenous administration of normal salt solution alternating with 10 per cent glucose in distilled water

CONTINUED BILIARY OBSTRUCTION —In order to prevent continued biliary obstruction a T tube is introduced at the time of the operation through this the duct system is washed out with ether or a combination of ether and ethyl alcohol Before the tube is removed a *cholangiogram* is advisable for demonstration of residual calculi or other forms of obstruction If all is well at the end of the second week the tube may be removed and the wound permitted to heal

POSTCHOLECYSTECTOMY SYNDROME —The postcholecystectomy syndrome consists in the persistence of symptoms following the removal of the gall sac Most often the complaints are pain in the right upper quadrant nausea postprandial distention and diffuse tenderness In some instances the disturbance may be due to associated *pancreatitis* (p 1941) *peptic ulcer* (p 1780) a *neoplasm* of the terminal portion of the common bile duct (p 1996) or *retention of stones* within the common duct (p 2004) Most often however the condition is a perpetuation of the preoperative *biliary dyskinesia* (p 2007) and it is treated in a similar manner The results however are rarely satisfactory For postoperative diet see p 688

EXTERNAL BILIARY FISTULA —External biliary fistulas occasionally occur spontaneously due to ulceration resulting from an impacted common duct stone More often however the condition is a postoperative complication and depends upon the failure to remove stones from the common duct or the development of a benign stricture The condition is associated with metabolic disturbances due to loss of bile salts calcium and the fat soluble vitamins particularly K (p 630)

With an external biliary fistula an attempt is made to replace the lost metabolites Eventually however a surgical procedure is required in the attempt to repair the damage and close the fistula Secondary operations on the biliary tract are associated with considerable operative risk a greater incidence of postoperative complications and many disappointments relative to closure of the fistula and the relief of associated symptoms

STRICTURE OF THE BILE DUCTS —Stricture of the bile duct may result from surgical interference or ulceration by a calculus Occasionally it fol

lows the inadvertent clamping of the common duct during cholecystectomy or gastrectomy

Following operation the patient with a stricture develops jaundice within the course of three to five months Occasionally this is relieved by the appearance of an external biliary fistula With incomplete obstruction secondary infection is inevitable at which time the closure becomes complete through the inflammatory edema

The biliary duct stricture requires operative interference If nothing else can be accomplished an anastomosis is performed between gallbladder and stomach or bowel



Fig 446—Congenital anomaly of the gallbladder (Phrygian cap)

CLINICAL DISTURBANCES

The clinical disturbances involving the gallbladder and the biliary ducts are as follows

- Congenital Abnormalities
  - Phrygian Cap
  - Atresia of the Biliary Duct
  - Choledochus Cyst
  - Congenital Bands
- Neoplasms
  - Of the Gallbladder
    - Benign
    - Malignant
  - Of the Bile Ducts
    - Benign
    - Malignant
  - Of the Papilla of Vater
- Metabolic Derangements
  - Cholelithiasis (Gallstones)
  - Choledocholithiasis
  - Cholesterosis ("Strawberry Gallbladder")
- Mechanical Lesions
  - Hydrops of the Gallbladder
  - Obstructive Jaundice
  - Biliary Dyskinesia (Dyssynergia)
- Infections
  - Acute Noncalculous Cholecystitis
  - Acute Calculous Cholecystitis
  - Chronic Noncalculous Cholecystitis ("Strawberry Gallbladder")
  - Chronic Calculous Cholecystitis
  - Suppurative Cholangitis and Choledochitis
  - Cholangitis Lenta
  - Parasitic Disease of the Biliary Ducts

CONGENITAL ABNORMALITIES OF THE GALLBLADDER

THE PHRYGIAN CAP AND OTHER CONGENITAL ABNORMALITIES

The Phrygian cap of the gallbladder produced by kinking or folding of the fundus occurs in 2 to 3 per cent of all individuals The anomaly

2086) *postoperative pneumonitis* (p 4016), continued *biliary obstruction* the *postcholecystectomy syndrome* (p 1992) *external biliary fistulas* and *strictures of the ducts*

SHOCK —Postoperatively jaundiced patients are prone to develop shock which can be controlled by transfusion If external biliary drainage has been established adequate fluid and salt intake must be maintained by the intravenous route until a full diet is tolerated since large amounts of salt are lost daily in the biliary drainage Not infrequently the *sodium loss* (p 729) in the biliary drainage on the fifth to eighth day after operation causes anorexia dehydration and a shock like picture with low blood pressure and a thready rapid pulse This condition dramatically responds to administration of saline intravenously

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on or about the tenth or twelfth day of life and an associated *hemorrhagic diathesis* bleedings may occur from the skin intestinal tract or cord The child usually succumbs within a month but may linger somewhat longer

Atresia of the bile duct requires differentiation from *physiological jaundice of the newborn* (p 2761) and *erythroblastosis foetalis* (p 1067) Neither of these conditions is associated with persistently acholic stools

Treatment —The only possible therapeutic approach to the problem of congenital obliteration of the bile duct is the surgical establishment of a lumen The operative procedure is a desperation remedy that is rarely successful because of its extensive technical nature and the poor condition of the patient

CHOLEDOCHUS CYST

The choledochus cyst is a rare congenital abnormality in which there is an ampulla like dilatation of the upper part of the common duct The condition may be completely *asymptomatic* but clinical manifestations may be encountered before the age of ten usually in girls

The symptoms of the choledochus cyst consist of episodes of *obstructive jaundice* (p 1953) associated with *fever leukocytosis* and *vomiting* pain tenderness and rigidity are noted in the *right upper quadrant* *cholecystograms* disclose an atypical shadow near the duodenum and flattening of the gallbladder

Treatment —In the presence of definite symptoms the choledochus cyst requires *surgical intervention* with the performance of a lateral choledochoduodenostomy the operative procedure is formidable and carries a high mortality

CONGENITAL BANDS

Congenital bands of peritoneum may stretch over the gallbladder or the common duct they may produce biliary stasis with or without obstructive jaundice The anomaly is diagnosed at operation and requires freeing if there are local symptoms

NEOPLASMS

BENIGN TUMORS OF THE GALLBLADDER

A papilloma of the gallbladder is noted in approximately 8 per cent of surgically removed sacs much less frequently the surgeon encounters *myomas lipomas fibromas myxomas* and *mixed tumors*

Papilloma of the Gallbladder —Papillomas of the gallbladder are usually small and multiple they are often found in association with *cholesterosis* (p 2005) and *chronic cholecystitis* (p 2010) Occasionally the papilloma is suspected when cholecystography reveals small oval or semicircular defects in the margin of the shadow of the gallbladder more often the gallbladder papilloma is not recognized until the operative procedure which is performed for symptoms referable to the associated condition

MALIGNANT TUMORS OF THE GALLBLADDER

Primary *sarcoma* of the gallbladder is a rare condition which produces early metastases and a fatal termination Primary *carcinoma* of the gall

has no clinical importance unless it is productive of *bile stasis* favoring the deposition of *calculi* (p 1997)

The patient with a Phrygian cap and persistent symptoms referable to the gallbladder is a candidate for *cholecystectomy* (p 1990)

Beside the Phrygian cap other congenital abnormalities of the gall bladder include congenital absence of the sac intrahepatic lodgment, the double gallbladder the floating gallbladder with a long mesentery and duplication of gallbladder and cystic duct The arteries are frequently un

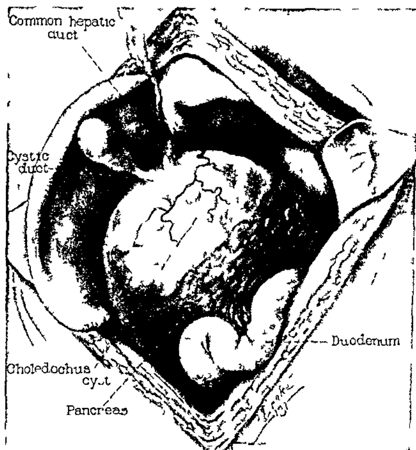


Fig 447—Choledochus cyst showing its appearance at operation (After Masson and Rieniets)*

usual in their distributions accessory cystic arteries are common and may occasionally produce mechanical difficulties

Congenital abnormalities do not require *treatment* unless there is super imposed stone formation (p 1997) or infection (p 2007)

ATRESIA OF THE BILIARY DUCTS

Obliteration of the *biliary ducts is a rare congenital abnormality* It is characterized by the onset of deep and progressive *jaundice* appearing

* Walters and Snell Diseases of the Gallbladder and Bile Ducts

METABOLIC DERANGEMENTS

CHOLELITHIASIS (GALLSTONES)

Because of its high incidence particularly in women cholelithiasis presents many important problem in clinical practice It is estimated that 5 to 6 per cent of adult postmortem examinations disclose the presence of gallstones Although only 10 per cent of calculous patients apparently suffer during their life times from clinical manifestations due to the biliary concretion nevertheless this group constitutes a large block of those who seek relief from gastro intestinal complaints

The Nat re of the Gallston —The essent al ingredients of the gallstone are cholesterol bilirubin and calcium alone or in combination

Cholesterol Stones—Pure cholest rol stones are radiotransparent they produce *negative shadows* in the visuali ed gallbladder and may be present as a s ngle huge concretion or as numerous small stones Their presence is sugg sted when m croscopic examination of material obtained by bil ary drainage discloses the characteristic crystals (p 3 26)

Calcium Stones—Calcium stones are usually reveal d by a *positive shadow* on the scout film most often they appear as the signet ring stone in which the rad opaque outer layer is a crust of calcium which encloses a rad otranslucent center most often representa ti e of a nucleus of cholest rol In the cholecystogram (p 2000) the radiotranslucent c nter of the signet ring stone may appear as a negative shadow

Bilirubin Stones—Gallstones made up of bile pigment are rarely encountered they cast *r diotr nslucent* shadows on the *cholecystogram* Most often the bilirubin calculus results from excessive bile p gment production as observed in the hemolytic anemias (p 1060) As in the instance of the chol sterol nucleus the b le pigment calculus may be encrusted with a shell of calcium

Et ology and P thogen s s—Systemic and local disturbances predispose to the formation of gallstones

System c Predisposition—The system c predispositions to gallstone formation include in fectious and metabolic disturbances *Bacteremias* part cularly during the course of *typho d fever* (p 22) may result in localization of pathogenic organisms within the gallbladder and later stone formation with a nest of viable organisms as a nucleus More often the systemic pr dispos tion is a *metabolic abnormality hypercholesteremia* (p ~36) *n obes ty pregnancy rap d weight loss* and *diabetes mellitus* favor the depos tion of crystals the *hemolytic anemias* (p 1060) with *portal hyperbil rub nemia* (p 19 1) may be followed by pre cipitation of bile p gment in the gallbladder and subsequent stone formation

Local Causes—The local disturbances which favor the deposition of gallstones may ar se in infect ous mechanical or metaboli derangements They include the *reflux of intes ti al content* into the biliary system as th result of insufficiency of the sphincter of Odd (p °007) *biliary stasis* due to spasm of the sph ncter (p 00) a congen tal abnormality (p 1994) an intrinsic defect of the du t sy tem or the result of pressure from without the deposit on of *cholesterol crystals* on the surface of the mucosa in *cholesterosis* (the strawberry g llbladder) (p 2005) a prec pitat on of cholesterol due to some change in the c n cent ation of b le salts and fa lure of the bladder wall to adjust the interchange of choles *terol between blood and gallbladder b le (p 1986)*

Pathology—The gallstone wh h dev lops as the re ult of a hyp rchol teremia (p ~36) or *hyperbil rubinemia* (p 19 1) may be demonstrable in a relat vely no mal gallbladder that wh ch follows upon a local inflammatory process is associated with the pathological lesions of *cute subacute* or *ch onic cholecyst tis* (p 2009) The l tter hanges may va y bet een the ongest on and leukocytic infiltrat on of an acute reaction to the atrophic and fibrot c ppearance of a chronic process

Strawberry Gallbladder—Midway between frankly metabolic and grossly inflammatory manifestations are the changes seen in the strawberry gallbladder In this condition the external appearance of the sac may be altered relatively littl When the gallbl dde is open d a characteristic speckled appearance is observed *yellow dots* represent areas of thick ened mucosa i filtrated with lipids and the intervening *red areas* are those in wh h the e mere congest on Approx mately 60 per cent of these strawberry gallbladders conta n con cretions

bladder also is infrequent it may develop on the basis of a preexistent papilloma or a concretion The histology of the gallbladder carcinoma is variable scirrhous papillary, colloid and squamous cell varieties have been described growth is rapid with early metastases in the liver and regional lymph nodes

The *clinical manifestations* of primary gallbladder malignancy are those of *local inflammation* or *obstructive jaundice* (p 1953) By the time the abdomen is explored the condition is inoperable and only palliation is possible

Metastatic malignancy of the gallbladder may accompany hepatic or peritoneal carcinomatosis There are no unusual diagnostic or therapeutic features

BENIGN TUMORS OF THE BILE DUCTS

Benign tumors of the bile ducts are rare a papilloma adenoma adeno fibroma lipoma or fibroma may be encountered when the patient is sur gically explored because of an *obstructive jaundice* (p 1953)

The benign tumor of the bile duct is not diagnosible except by ex ploratory laparotomy the lesion is excised if possible

MALIGNANT TUMORS OF THE BILE DUCTS

A malignant tumor of the bile ducts is a rare type of neoplasm unlike other lesions of the biliary passages which predominate in females they are encountered twice as frequently in *males*

Malignancy of the bile duct is most often *carcinomatous* the cell type may be columnar or spheroidal the growth appears as a villous diffuse or nodular neoplasm and produces the clinical manifestations of an *obstruc tive jaundice* (p 1953) By the time laparotomy is performed spread has occurred to liver regional lymph nodes pancreas and distant organs such as the lungs A palliative *anastomosis* between gallbladder and intestine may relieve the jaundice

CARCINOMA OF THE AMPULLA OF VATER

Carcinoma of the ampulla of Vater differs from the malignancies of the gallbladder and bile ducts in that the clinical features are rather char acteristic operative removal may be within the bounds of possibility

With a malignant lesion of the ampulla the patient complains of *local pain* there may be intermittent attacks of *jaundice* (p 1951) the icterus clearing when the obstruction is relieved through ulceration of the neo-plasm In almost every instance Courvoisier s law is demonstrated in that *hydrops of the gallbladder* (p 2006) is noted Cholecystograms may reveal obstruction at the level of the ampulla filling defects in this area flatten ing of the duodenum from behind and irritability of the second portion of the duodenum Occult blood is present in stools

The management of the condition can only be approached surgically successes have been reported by two stage operations which accomplish removal of the tumor the lower end of the common duct and the head of the pancreas occasional survivals for several years have been encoun tered

METABOLIC DERANGEMENTS

CHOLELITHIASIS ("GALLSTONES")

Because of its high incidence particularly in women cholelithiasis presents many important problems in clinical practice It is estimated that 5 to 6 per cent of adult postmortem examinations disclose the presence of gallstones Although only 10 per cent of calculous patients apparently suffer during their life times from clinical manifestations due to the biliary concretion nevertheless this group constitutes a large block of those who seek relief from gastro intestinal complaints

The Nature of the Gallstone—The essential ingredients of the gallstone are cholesterol, bilirubin and calcium alone or in combination

Cholesterol Stones—Pure cholesterol stones are radiotransparent they produce *negative shadows* in the visualized gallbladder and may be present as a single huge concretion or as numerous small stones Their presence is suggested when microscopic examination of material obtained by biliary drainage discloses the characteristic crystals (p 3 6)

Calcium Stones—Calcium stones are usually revealed by a *positive shadow* on the scout film most often they appear as the "signet ring" stone in which the radiopaque outer layer is a crust of calcium which encloses a radiotranslucent center most often representative of a nucleus of cholesterol In the cholecystogram (p 2000) the radiotranslucent center of the "signet ring" stone may appear as a negative shadow

Bilirubin Stones—Gallstones made up of bile pigment are rarely encountered they cast *radiotranslucent* shadows on the *cholecystogram* Most often the bilirubin calculus results from excessive bile pigment production as observed in the hemolytic anemias (p 1060) As in the instance of the cholesterol nucleus the bile pigment calculus may be encrusted with a shell of calcium

Etiology and Pathogenesis.—Systemic and local disturbances predispose to the formation of gallstones

Systemic Predisposition—The systemic predispositions to gallstone formation include infectious and metabolic disturbances *Bacteremias* particularly during the course of *typhoid fever* (p 225) may result in localization of pathogenic organisms within the gallbladder and later stone formation with a nest of viable organisms as a nucleus More often the systemic predisposition is a *metabolic abnormality hypercholesteremia* (p 736) *in obesity pregnancy rapid weight loss* and *diabetes mellitus* favor the deposition of crystals the *hemolytic anemias* (p 1060) with *portal hyperbilirubinemia* (p 1951) may be followed by precipitation of bile pigment in the gallbladder and subsequent stone formation

Local Causes—The local disturbances which favor the deposition of gallstones may arise in infectious mechanical or metabolic derangements They include the *reflux of intestinal content* into the biliary system as the result of insufficiency of the sphincter of Oddi (p 2007) *biliary stasis* due to spasm of the sphincter (p 200) a congenital abnormality (p 1991) an intrinsic defect of the duct system or the result of pressure from without the deposition of *cholesterol crystals* on the surface of the mucosa in *cholesterosis* (the strawberry gallbladder) (p 200) a precipitation of cholesterol due to some change in the concentration of bile salts and failure of the bladder wall to adjust the interchange of cholesterol between blood and gallbladder bile (p 1990)

Pathology—The gallstone which develops as the result of a hypercholesteremia (p 36) or *hyperbilirubinemia* (p 1951) may be demonstrable in a relatively normal gallbladder that which follows upon a local inflammatory process is associated with the pathological lesions of *acute subacute* or *chronic cholecystitis* (p 2009) The latter changes may vary between the congestion and leukocytic infiltration of an acute reaction to the atrophic and fibrotic appearance of a chronic process

Strawberry Gallbladder—Midway between frankly metabolic and grossly inflammatory manifestations are the changes seen in the strawberry gallbladder In this condition the external appearance of the sac may be altered relatively little When the gallbladder is opened a characteristic speckled appearance is observed *yellow dots* represent areas of thickened mucosa infiltrated with lipids and the intervening *red areas* are those in which there is more congestion Approximately 60 per cent of these strawberry gallbladders contain con

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The management of the condition can only be approached *surgically* successes have been reported by two stage operations which accomplish removal of the tumor the lower end of the common duct and the head of the pancreas occasional survivals for several years have been encoun tered

[illegible] —The pathology of cholelithiasis is [illegible] limited to the changes [illegible] in the gallbladder alone. [illegible] [illegible] with the [illegible] of a biliary [illegible] (p. [illegible]). Additionally there may appear [illegible] of the complications such as empyema or [illegible] of the gallbladder, [illegible] or perforation of the [illegible] [illegible] or [illegible]

Clinical Manifestations.—Uncomplicated cholelithiasis is essentially an asymptomatic disorder, the appearance of symptoms resulting as some mechanical defect or the result of reflex changes.

Asymptomatic Cholelithiasis.—The histories of patients whose autopsies reveal cholelithiasis indicate that only 10 per cent seem to have suf-



Fig 449.—Asymptomatic cholelithiasis. Note nest of signet-ring shadows due to radiotranslucent cholesterol cores and radiopaque calcium crusts. Also solitary stone in ampulla. No change in shadows over observation period of eighteen years. Patient died at age of 67 of cerebral thrombosis.

fered from the presence of their gallstones. It must be assumed therefore that 90 per cent of those with uncomplicated cholelithiasis pursue an asymptomatic course or one which is associated with only minor distress.

Reflex Gastro-intestinal Manifestations.—Cholelithiasis is most frequently associated with the reflex *gastro intestinal neuroses*, often with an accompanying *gastritis* (p. 1808) or *duodenitis* (p. 1813). Thus the clinical manifestations are those of *dyspepsia* (p. 1770) or *peptic ulcer* (p. 1780). The patient may have hyperacidity, anacidity, hypomotility, hypermotility or pylorospasm; others display the syndrome of reverse peristalsis with

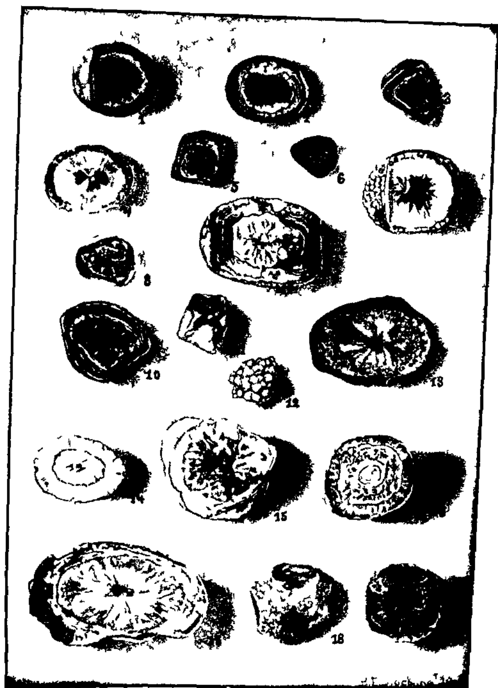


Fig 418—Gallstones of various types cut and polished 4 7 13 14 and 17 are primary gallstones at first composed of almost pure cholesterine later covered with pigment 3 5 6 and 11 are faceted secondary stones 9 and 10 show well the thin laminae found under the faceted surfaces

* MacCallum Textbook of Pathology

the organ is enlarged when visualization is poor or absent and with delayed emptying or persistent irregularities

Course and Complications—As has been previously emphasized cholelithiasis usually pursues an uncomplicated and asymptomatic course When difficulties arise they are due to mechanical disturbances or infections

Mechanical Disturbances—The mere mechanical presence of a gallstone is capable of producing a variety of local complications quite aside from the factor of infection Migration of a small stone or the fragment of a large one into the duct system produces *biliary colic* interference with the evacuation of the sac results in *biliary stasis* inviting further precipitation of salts and infection complete occlusion of the cystic duct gives a *hydrops* (p 2006) provided the gallbladder wall is still capable of distention interference with the neuromuscular control of the sphincter of Oddi produces *biliary dyskinesia* (p 2007) which may result in insufficiency and reflux of intestinal bacteria (p 1986) or spasm and biliary stasis (p 1987) Transfer of the stone to the common duct occurs in *choledocho*



Fig 4 0—Normally functioning gallbladder with cholesterol stones

lithiasis (p 2004) irritation of the wall may predispose to *malignant transformation* or result in *ulceration perforation* the production of a *fistula* into another intra abdominal viscus or an *intestinal ileus* (p 1873)

Infection—Infection of the gallbladder (cholecystitis) may precede or follow the formation of the concretion The inflammatory process may be acute subacute or chronic attacks are often recurrent and may be complicated by *necrosis gangrene* or *perforation* (p 2009) Each of the latter is associated with spreading infections such as localized or generalized *peritonitis* (p 1928) *hepatitis* (p 1979) *liver abscess* (p 1980) *subphrenic abscess* (p 1928) *cholangitis* (p 2010) *pancreatitis* (p 1939) or *pylephlebitis* (p 1961)

Diagnosis—The diagnosis of cholelithiasis presents a dual problem it is first necessary to establish the presence of the stone and then evaluate the relationship between the findings and the clinical manifestations

The diagnosis of gallstone disease is strongly suspected when the middle aged woman develops gastro intestinal symptoms The presumption is

Walters and Snell Diseases of the Gallbladder and Bil Ducts

epigastric pressure and fullness nausea salivation vomiting belching and water brash', there may be spastic or atonic constipation or attacks of diarrhea

The protean nature of gallstone disease emphasizes the importance of suspecting biliary concretions in each patient who complains of gastro in testinal symptoms The wary physician never commits himself to a diag nosis of any digestive disorder without a complete investigation of the gall sac and the biliary passages

Reflex Circulatory Manifestations —There is increasing awareness of a relationship between cholelithiasis and the circulatory phenomena of *angina pectoris* (p 890) and the *cardiac arrhythmias* (p 873) The association is *demonstrable by the therapeutic test when cholecystectomy is followed by* relief of the cardiac derangements

Biliary Colic —The characteristic symptomatic picture of a typical bili ary colic consists of a severe *pain* in the right upper quadrant (p 1959) associated with *nausea* and *vomiting* but little or no elevation of tem perature Characteristically the pain radiates to the back and right shoul der less often it is referred to the *left upper quadrant* (p 1942) and pre cordium (p 892) suggesting the *anginal syndrome* (p 890) or a *coronary occlusion* (p 983)

Biliary colics occur at irregular intervals and may be associated with *transitory mild icterus* examination at most reveals tenderness in the right upper quadrant and increased sensitivity of the right trapezius

Physical Examination —The physical examination in uncomplicated chole lithiasis is most uninformative The patient is usually an obese and flabby multipara often there are *xanthelasmas* (p 3243) of the eyelids during an acute attack there may be some tenderness in the right upper quad rant particularly at *Murphy s point* just below the costal margin in the midclavicular line When the examining fingers are hooked deep beneath the costal arch the patient is unable to take a deep breath without the production of severe pain As a manifestation of the phrenic reflex there may be *tenderness of the right trapezius*

Occasionally an enlarged gallbladder is palpable but a chronic hy drops is more suggestive of neoplastic obstruction at the papilla of Vater (p 1996)

Laboratory Data —In the majority of instances uncomplicated chole lithiasis is a laboratory diagnosis Suggestive evidence is afforded by ex aminations of the blood and duodenal contents the former reveals a *hypercholesteremia the duodenal content is characterized by absence of B bile* after the intraduodenal administration of olive oil or 33 per cent magnesium sulfate and a sediment which contains *cholesterol crystals pus bile stained epithelium* or *deposits of amorphous pigment*

Roentgenograms —The positive diagnosis of cholelithiasis is established by roentgenograms *Scout films* clearly reveal radiopaque calculi of cal cium or the signet ring appearance when a radiotranslucent nucleus is encrusted with a shell of lime

CHOLECYSTOGRAPHY —The most valuable information is obtained from cholecystography after the use of the specific gallbladder dye Positive and incontrovertible evidence includes negative shadows which result from the presence of radiotranslucent calculi presumptive evidence is afforded when

3 The superimposition of *infection* in the nature of a cholecystitis (p 2009) or a cholangitis (p 2010)
4 The development of *malignant degeneration*
5 The development of *organic disease* in nearby structures including *peptic ulceration hepatitis biliary cirrhosis* and *pancreatitis*
6 The development of *cardiovascular complications* including *angina pectoris* (p 890) and the *arrhythmias* (p 873)

The Details of Medical Treatment—Medical treatment of gallstones is limited to attempts to provide symptomatic comfort and the avoidance of complications

Diet—We favor the use of a bland *high carbohydrate low fat intake* (p 672) this diet is intended for weight reduction rather than the pre vention of further precipitation within the bladder Evacuation of the gall bladder is encouraged by ordering the patient to take a tablespoon of olive oil cream or egg yolk about a half hour before each principal meal

Digestive Symptoms—Accompanying gastro intestinal disturbances are symptomatically managed Patients with low acid figures are given hydro chloric acid (p 1740) those with hyperacidity are advised to take antacids (p 1754) muscle spasms are treated with Mistura Nigra (p 1757) accom panied by an antispasmodic (p 3875) Patients with a tendency to con stipation are often benefited by the administration of a saline laxative each morning

Duodenal and Transduodenal Lavage (*Nonsurgical Drainage*)—We have no great faith in duodenal lavage or transduodenal feedings we be lieve that just as much relaxation of the sphincter of Oddi is accomplished by the oral ingestion of olive oil or 33⅓ per cent magnesium sulfate as can be accomplished by means of the duodenal tube

Bile Salts and Biliary Antiseptics—We place no great reliance on the administration of bile salts to gallstone patients their greatest efficacy in our experience is their laxative action and their appeal to the imagination of the patient Neither do we recommend the use of the *biliary antiseptics* in uncomplicated cholelithiasis

Spa Treatment and Diathermy—We have no faith in *diathermy* de spite the claims of enthusiasts We do not think that anything is accom plished by *spa treatment* (p 3764) beyond the mechanism of escape

Indications for Surgery—There is an increasing tendency to refer the patient with gallstones to the surgeon Absolute indications for surgery include

1 The presence of *persistent reflex gastro intestinal symptoms*
2 The presence of *infection*
3 The presence of *complications*
4 Repeated attacks of *biliary colic*
5 The presence of pus or red cells in the *duodenal contents*
6 The presence of abnormalities in the *cholecystogram*
7 The presence of a *palpable gallbladder*
8 The presence of *persistent local tenderness or rigidity* pointing to peritoneal irritation
9 The suspicion of an accompanying *choledocholithiasis* (p 2004)

verified by laboratory data which include positive findings in the *duodenal contents* and the radiographic evidences obtained by the *scout film* and *cholecystography* (p 2000)

It requires a nicety of clinical judgment to assay the relationship between the demonstrable gallstone and the presenting symptoms The initial problem involves elimination of the presence of other digestive disorders such as *peptic ulcer* (p 1780) or *gastric malignancy* (p 1815) Roentgenological studies are mandatory before the expression of an opinion If gastric malignancy is suspected gastric contents show complete achylia and stool tests are repeatedly positive for occult bleeding Often the problem is settled only at exploration

Treatment

The management of gallstones may be attempted by medical or surgical measures The former only succeeds in affording symptomatic relief and the prevention of complications it is only by operative procedure that the condition is attacked with any degree of satisfaction and any promise of success

Non operative Treatment—Conservative management is warranted under the following circumstances

1 The disturbance is *asymptomatic*
2 The *duodenal contents* fail to show evidences of suppuration (leukocytes) or ulceration (erythrocytes)
3 The *cholecystogram* reveals relatively slight impairment of visualization concentration or evacuation
4 The episodes of *biliary colic* are infrequent mild and unaccompanied by significant fever or jaundice
5 The *reflex gastro intestinal or cardiovascular manifestations* are controlled by symptomatic therapy
6 For reasons other than biliary the patient is a *bad surgical risk* (p 3997)
7 The patient is reluctant to submit to a surgical procedure
8 There are not present and have not been present complications either mechanical or infectious
9 The possibility that the symptoms are due to a *biliary dyskinesia* which anteceded the formation of the stones These patients when subjected to surgery, often suffer from the *postcholecystectomy syndrome* (p 1992)

Dangers of Conservatism—The conservative treatment of gallstones may engender more risk to the patient than the hazards of operative surgery There is no way of estimating when a dormant situation will flare into activity with irreparable damage and increase in *surgical morbidity mortality* and postoperative complications

The dangers of conservatism are as follows

1 Continuation of *biliary stasis* with the formation of more stones
2 The occurrence of *mechanical complications* such as hydrops ulceration and choledocholithiasis (p 2004)

spicuously absent *splenomegaly* is rarely encountered unless there is an accompanying obstructive biliary cirrhosis the *urine* contains albumin casts and bile pigments the *stool* is acholic the *hemogram* gives evidence of a polymorphonuclear leukocytosis the *sedimentation rate* is increased *serum bilirubin figures* are elevated there is temporary retention of brom sulfalein but the other biliary function tests are not consistently altered

Diagnosis —See *Jaundice* (p 1951) *Pain in Right Upper Quadrant* (p 1959)

Treatment —The treatment of common duct stone is urgently surgical combined and intensive parenteral treatments with streptomycin (p 104) and penicillin (p 106) are begun an intravenous drip is set up on return from the operating room for the delivery of water salt dextrose plasma and/or whole blood

CHOLESTEROSIS (STRAWBERRY GALLBLADDER CHRONIC NONCALCULOUS CHOLECYSTITIS)

For present purposes cholesterosis is regarded as a local metabolic ab normality the chronic inflammatory changes in the gallbladder are looked



Fig 451 —*a* Simple chronic catarrhal cholecystitis *b* chronic catarrhal cholecystitis with cholesterosis (strawberry gallbladder) *c* chronic catarrhal cholecystitis with papillomas *d* chronic catarrhal cholecystitis with cholesterosis and papilloma

upon as the result of the depositions of cholesterol in the mucous mem brane As has been elsewhere stated there is excellent ground for con sidering the chronic cholecystitis as the primary local condition with the cholesterol depositions as a result of the inflammatory process

Pathology —See p 1997

Clinical Manifestations —Before the formation of demonstrable calculi the clinical manifestations of cholesterosis are identical with those of a *biliary dyskinesia* (p 2007) Clinical and laboratory examinations includ ing cholecystography (p 2000) reveal no significant abnormality and the patient is subjected to surgery because of the persistence of symptoms At laparotomy the gallbladder appears grossly normal in the majority of instances and it is only when it has been removed and opened that the characteristic strawberry appearance is observed

After calculi have formed in the strawberry gall bladder the pre senting symptoms are those of *cholelithiasis* (p 1997) with its characteris tic findings in the *duodenal contents* the *scout films* and *cholecystograms*

* Walters and Snell Diseases of the Gallbladder and Bile Ducts

10 The suspicion of *malignancy*
11 The suspicion of accompanying damage in the *pancreas liver stomach* or *duodenum*
12 The possibility that an *angina pectoris* or *cardiac arrhythmia* may result from reflex irritation

Procedure —The operative procedure of election in cholelithiasis is obviously a *cholecystectomy* (p 1991) Preoperative medications and post operative management are elsewhere discussed (p 1990) The practitioner is cautioned to renew medical therapy following operation lest a *post cholecystectomy syndrome* result from persistence or aggravation of the *biliary dyskinesia* (p 2007)

CHOLEDOCHOLITHIASIS

The patient with cholelithiasis has an estimated 13 to 20 per cent chance of having an associated choledocholithiasis The common duct stone may be of gallbladder origin or it may have developed in situ since gallstones form wherever there is bile as illustrated by incrustations on drainage tubes utilized postoperatively in the biliary passages

In the majority of instances a single stone is found in the common duct but large numbers occasionally are encountered Most often the common duct calculus is present in the terminal portion

Pathology —The common duct stone produces a variety of changes in the local structures These include dilatation of the extrahepatic bile passages impaction with the development of *obstructive jaundice* (p 1953) superimposed infection with *cholangitis* (p 2010) and the *Charcot fever* local ulceration of the wall which may lead to *perforation* and *fistulization* increased intraductal pressure producing changes in the liver incomplete closure of the sphincter of Oddi inviting infection by the intestinal micro organisms reflux into the pancreas predisposing to *acute and chronic pancreatitis* (p 1941) suppression of the excretory functions of the liver in respect to bilirubin with the production of white bile

Clinical Manifestations —Choledocholithiasis may be *asymptomatic* this observation requires exploration of the common duct during the course of each cholecystectomy (p 1991)

The clinical phenomenon attributed to the uncomplicated common bile duct stone may be indistinguishable from those produced by *biliary dyskinesia* (p 2007) and *cholelithiasis* (p 1997) After the gallbladder has been removed persistence of symptoms indicates the likelihood of an over looked stone in the common duct

Intermittent Hepatic Fever (Charcot Fever) —With an impacted stone in the common duct and cholangitis the patient complains of *acute attacks* of *biliary colic* with *jaundice chills* and *fever* the *urine* is noted to be dark while the *stools* are acholic When the stone is floated back into the dilated duct the obstruction is relieved and the symptoms dissipate only to recur shortly when the duct is again occluded Since the gall bladder is atrophic in the vast majority of instances *hydrops does not occur* thus differentiating the *condition from that of* carcinoma of the head of the pancreas (p 1943)

Physical examination in Charcot fever reveals little of value other than the presence of fever and jaundice there may be some localized tenderness in the right upper quadrant hydrops of the gallbladder is con

tremely protracted obstruction results in abnormalities of calcium metabolism as revealed by an osteoporosis (*hepatic rickets*)

BILIARY DYSKINESIA (DYSSYNERGIA)

Disturbances in the biliary kinetics are of great clinical significance *inadequate sphincteric control* permits a constant leakage of liver bile into the intestines without concentration in the gallbladder it results in a reflux of intestinal organisms and bacteria into the normally sterile hepatic radicles and may produce a cholecystitis (p 2007)

Increase in the intrabiliary pressure accompanies *spasm of the sphincter of Oddi* This functional manifestation of a biliary dyskinesia predisposes to *biliary stasis* and the formation of *gallstones* (p 1997) Sphincteric spasm may be *neurogenic* comparable to a pylorospasm it may be a *reflex* as a result of a local lesion in the stomach duodenum gallbladder or pancreas it may be *psychogenic* as in emotional jaundice

Clinical Manifestations —The patient with a spasmodic biliary dyskinesia complains of dull *pain* which occurs as long as two hours following meals The distribution is that of a gallstone colic (p 2000) there may be radiation to the epigastrium or to the left nausea and vomiting occur with some frequency occasionally a subicteric tint is noted in the cornea usually there is some associated disturbance in the bowel habits (constipation or diarrhea) Tenderness is often present in the right hypochondrium or the epigastrium

Acute spasm may result in emotional jaundice or bilious vomiting

Diagnosis —The diagnosis of biliary dyskinesia can be arrived at only by exclusion of the presence of organic disease Gastric and duodenal analyses should reveal no significant abnormality the stools must be free from blood bile pigment must not be demonstrable in the urine serologic tests for bilirubin and liver function tests must be normal Cholecystography must reveal a gallbladder of normal appearance with good filling and concentration but there may be some delay in emptying

Treatment —Acute attacks of spasm of the sphincter of Oddi are not relieved by morphine but respond well to *nitrites* (p 3892) intravenous injections of *papaverine* (p 3859) and the subcutaneous use of *demerol* (p 3863)

In the interval between attacks associated gastro intestinal abnormalities are corrected *dilute hydrochloric acid* is given to those with achylia (p 1740) *antacids* (p 1754) are prescribed for patients with hyperacidity gastric sedation with *Mistura Nigra* (p 1757) is valuable under all circumstances the *antispasmodics* (p 3875) such as trasentin merit a trial constipation is corrected and diarrhea is controlled through dietary principles (p 668)

The practitioner is wary lest the functional aspects lull him into a false sense of security roentgenograms and cholecystograms are repeated at frequent intervals for information pertaining to changes in the organic status of the extrabiliary passages

INFECTIONS

ACUTE NONCALCULOUS CHOLECYSTITIS

Acute noncalculous cholecystitis is an infrequent clinical entity It may be encountered as the result of *hematogenous infection* or some *local vas*

The calculous disease is indication for operation often the diagnosis of the fundamental lesion is not established until the *gallbladder is opened*

Treatment—The patient with minimal symptoms and no demonstrable calculi is usually treated in the manner of a *biliary dyskinesia* (p 2007) If there are surgical indications for intervention *cholecystectomy* is performed Unfortunately residual symptoms are frequently encountered in the nature of the *postcholecystectomy syndrome* probably due to the biliary dyskinesia which may have antedated the cholesterosis (p 1992)

Mechanical Lesions

HYDROPS OF THE GALLBLADDER

Obstruction of the cystic duct may result in hydrops of the gallbladder This abnormality arises from the presence of a *foreign body* particularly a *gallstone* from *strictures* due to intrinsic changes within the wall or from pressure from without The damaged gallbladder *is not capable of* significant distention hence the condition is not observed in common duct stone associated with *chronic cholecystitis* (p 2010) Hydrops occurs most characteristically with *carcinoma of the head of the pancreas* (p 1943) as an illustration of *Courvoisier s law*

BILIARY OBSTRUCTION AND POSTHEPATIC JAUNDICE

In the main discussion of jaundice (p 1951), three varieties of icterus are described *prehepatic jaundice* is usually due to excessive hemolysis *true hepatic jaundice* follows injuries to the liver cells *posthepatic jaundice* the present concern results from obstruction of bile in the biliary passages

When intrabiliary pressure equals or exceeds the secretory pressure within the liver cells the secretion of bile is depressed or suppressed the bile then passes from the biliary canaliculi through the liver cells and into the hepatic veins (*regurgitation jaundice*) With depression of the secretion of bile substances which lower surface tension enter the blood in high concentration thus altering the directly positive phase of the *van den Bergh reactions* (p 1947) In most instances *long continued increased* intrabiliary pressure produces necrosis of liver cells and the features of *hepatic jaundice* are added to those of the obstructive jaundice

The Effects of Posthepatic Jaundice—With posthepatic jaundice the mucous membranes and the skin assume a greenish tint the presence of bile salts in the blood produces pruritus and bradycardia

The laboratory data report hyperbilirubinemia a direct positive van den Bergh reaction increase of blood cholesterol and cholesterol ester elevated serum phosphatase (p 1948) and a negative cephalin flocculation test unless there *is associated liver damage bile pigments are grossly apparent* in the urine but urobilin is absent unless there is superimposed biliary tract infection when bacteria reduce large amounts of bilirubin to urobilin within the biliary system the stools are bulky fatty and acholic they have an offensive odor

Exclusion of bile from the intestinal tract produces profound metabolic effects the absorption of calcium and the fat soluble vitamins (A D E and K) is impaired these disturbances are reflected by a prolongation of the prothrombin time (p 1109) and a *hemorrhagic tendency* (p 630) Ex

tremely protracted obstruction results in abnormalities of calcium metabolism as revealed by an osteoporosis (*hepatic rickets*)

BILIARY DYSKINESIA (DYSSYNERGIA)

Disturbances in the biliary kinetics are of great clinical significance *inadequate sphincteric control* permits a constant leakage of liver bile into the intestines without concentration in the gallbladder it results in a reflux of intestinal organisms and bacteria into the normally sterile hepatic radicles and may produce a cholecystitis (p 2007)

Increase in the intrabiliary pressure accompanies *spasm of the sphincter of Oddi* This functional manifestation of a biliary dyskinesia predisposes to *biliary stasis* and the formation of *gallstones* (p 1997) Sphincteric spasm may be *neurogenic* comparable to a pylorospasm it may be a *reflex* as a result of a local lesion in the stomach duodenum gallbladder or pancreas it may be *psychogenic* as in emotional jaundice

Clinical Manifestations—The patient with a spasmodic biliary dyskinesia complains of dull *pain* which occurs as long as two hours following meals The distribution is that of a gallstone colic (p 2000) there may be radiation to the epigastrium or to the left nausea and vomiting occur with some frequency occasionally a subicteric tint is noted in the cornea usually there is some associated disturbance in the bowel habits (constipation or diarrhea) Tenderness is often present in the right hypochondrium or the epigastrium

Acute spasm may result in emotional jaundice or bilious vomiting

Diagnosis—The diagnosis of biliary dyskinesia can be arrived at only by exclusion of the presence of organic disease Gastric and duodenal analyses should reveal no significant abnormality the stools must be free from blood bile pigment must not be demonstrable in the urine serologic tests for bilirubin and liver function tests must be normal Cholecystography must reveal a gallbladder of normal appearance with good filling and concentration but there may be some delay in emptying

Treatment—Acute attacks of spasm of the sphincter of Oddi are not relieved by morphine but respond well to *nitrites* (p 3892) intravenous injections of *papaverine* (p 3859) and the subcutaneous use of *demerol* (p 3863)

In the interval between attacks associated gastro intestinal abnormalities are corrected *dilute hydrochloric acid* is given to those with achylia (p 1740) *antacids* (p 1754) are prescribed for patients with hyperacidity gastric sedation with *Mistura Nigra* (p 1757) is valuable under all circumstances the *antispasmodics* (p 3875) such as trasentin merit a trial constipation is corrected and diarrhea is controlled through dietary principles (p 668)

The practitioner is wary lest the functional aspects lull him into a false sense of security roentgenograms and cholecystograms are repeated at frequent intervals for information pertaining to changes in the organic status of the extrabiliary passages

INFECTIONS

ACUTE NONCALCULOUS CHOLECYSTITIS

Acute noncalculous cholecystitis is an infrequent clinical entity It may be encountered as the result of *hematogenous infection* or some *local vas*

cular abnormality The latter includes *embolizations of the cystic arteries* which may occur in *subacute bacterial endocarditis* (p 1021) or following an *acute appendicitis* (p 1881) The local vascular injury may be in the nature of an *arteriosclerotic closure* (p 976) or a consequence of *periarteritis nodosa* (p 1027) *Hematogenous cholecystitis* has been described in bacteriemia due to *typhoid or colon bacilli streptococci staphylococci* and *pneumococci*

Clinical Manifestations —Acute noncalculous cholecystitis is marked by fever chilling leukocytosis and prostration in a patient with slight icterus *pain tenderness and rigidity in the right hypochondrium* Roentgenograms provide little information since calculi are not demonstrable on the scout



Fig 4?? —Nonfunctioning gallbladder with stones and small amount of milk of calcium bile at fundus stone in cystic duct

film and cholecystography is impracticable because of the condition of the patient

Course —Acute noncalculous cholecystitis has a strong tendency toward *spontaneous subsidence* In less favorable instances there may be serious complications such as gangrene penetration or perforation of the sac peritonitis pylephlebitis subphrenic abscess or cholangitis

Diagnosis —See *Pain in Right Upper Quadrant* (p 1959)

Treatment —We favor *urgent surgery* as soon as the diagnosis of acute cholecystitis is established Because of the possibility of a pre existent or a complicating bacteriemia we advocate preoperative and postoperative chemotherapy using *streptomycin* (p 104) and *penicillin* (p 106) either

alone or in combination The procedure of election is a *cholecystectomy* (p 1990)

ACUTE CALCULOUS CHOLECYSTITIS

Acute calculous cholecystitis is a complication of cholelithiasis rather than an independent clinical entity

Clinical Manifestations—In the patient with known cholelithiasis the complication of acute chloecystitis is suspected when there is an acute febrile episode with slight jaundice and localizing manifestations in the right upper quadrant (p 1959) The patient notes pain the examiner finds localized tenderness and rigidity a leukocytosis is reported from the laboratory and the sedimentation time may be markedly increased

Diagnosis—See *Pain in Right Upper Quadrant* (p 1959)

Course and Complications—Acute calculous cholecystitis often subsides with later chronic changes in the wall of the sac The lesion may progress to complicated phenomena such as pericholecystitis ulceration and gangrene of the sac localized or generalized peritonitis subphrenic abscess pylephlebitis and cholangitis

Pericholecystitis—Pericholecystitis is an integral part rather than a complication of acute cholecystitis The serous surface invariably shows the presence of fibrin when the acute process subsides enveloping adhesions may be encountered producing mechanical abnormalities in the gall bladder stomach and duodenum

Hydrops and Empyema of the Gallbladder—Before atrophic changes have occurred in the wall of the gallbladder the viscus is capable of distention and a localized tumor may be palpable With secondary infection an empyema develops with more violent pain tenderness and rigidity and more severe constitutional manifestations

Ulceration and Gangrene of the Gallbladder—With ulceration and gangrene of the acutely inflamed gallbladder there may be the same deceptive symptoms that accompany similar complications in acute appendicitis (p 1881) Local pain tenderness and rigidity subside but the general condition of the patient deteriorates with progressive prostration tachycardia and evidences of peripheral vascular failure The temperature may be deceptively lower but the experienced practitioner recognizes that the clinical condition is progressing in a manner that is far from satisfactory

External and Internal Biliary Fistulas—With rupture of the gallbladder external and internal fistulas may form The former are easily recognized but the latter are usually recognized only at diagnostic laparotomy

Localized or Diffuse Peritonitis—Localized peritonitis in the region of the acutely inflamed gallbladder occurs when there is intense inflammation of the wall with penetration but no actual perforation Perforative lesions are more apt to be associated with a generalized soiling of the peritoneal cavity

The symptoms and signs of the peritonitis are elsewhere described (p 1923)

Hepatitis and Pancreatitis—See p 1939

Subphrenic Abscess—See p 1928

Pylephlebitis—See p 1061

Acute Cholangitis—See p 2010

Treatment—We advocate *urgent surgery* in the presence of an acute calculous cholecystitis the procedure of choice is a cholecystectomy (p 1991) preoperative and postoperative measures of therapy are elsewhere outlined (p 1990)

CHRONIC NONCALCULOUS CHOLECYSTITIS

See *Cholesterosis* (*The Strawberry Gallbladder*) (p 2005)

CHRONIC CALCULOUS CHOLECYSTITIS

Chronic inflammations of the gallbladder with or without cholelithiasis (p 1997) often result in marked thickening of the viscus which may go on to atrophy that is so extreme that the sac is reduced to a mere fibrous cord

The diagnosis of chronic cholecystitis is based upon complete failure of the organ to visualize in a patient who has a previous history of *cholelithiasis* (p 1997) or *cholecystitis* (p 2009)

Chronic calculous cholecystitis may be treated with hydrocholeretics (p 1989) If there are manifestations relative to the cholelithiasis or choledocholithiasis (p 2004) operative interference is required

SUPPURATIVE CHOLANGITIS OR CHOLEDOCHITIS

Suppuration of the common bile duct and the biliary radicals is associated with the impaction of stones and infection The presenting symptoms are those of *intermittent hepatic fever* (Charcot s syndrome) as elsewhere described (p 2004) A feature of this condition is the illustration of *Courvoisier s law* in which hydrops of the gallbladder fails to occur due to the associated presence of a chronic cholecystitis with atrophy

Treatment—Suppurative cholangitis or choledochitis is an urgently surgical problem Combined and intensive parenteral treatment with streptomycin (p 104) and penicillin (p 106) are begun

CHOLANGITIS LENTA

A chronic type of cholangitis may be the result of a generalized *Streptococcus viridans bacteremia* (p 1021) less frequently the condition is associated with a generalized sepsis in *pneumonia influenza* or *typhoid fever* (p 225)

Clinical Manifestations—The clinical manifestations of cholangitis lenta combine those of a *bacteremia* with evidences of *obstructive jaundice* (p 1953) The patient has protracted pyrexia frequent *chilling and icterus* the liver is enlarged and tender there may be splenomegaly and clubbing of the fingers

Blood cultures reveal the presence of the causative organism Anti infective therapy is instituted with great vigor using streptomycin (p 104) and penicillin (p 106) concurrently

PARASITIC DISEASE OF THE BILE DUCTS

Parasites may become impacted in the common bile duct and give the evidences of an obstructive jaundice (p 1953) *Ascaris lumbricoides* (p 1906) *echinococcus* (p 1983) *liver flukes* (p 1982) *Giardia lamblia* (p 1892) and *Taenia saginata* (p 1899) have been demonstrated in occasional instances

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